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# TROPICAL DISEASES BULLETIN

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

# TROPICAL DISEASES BULLETIN.

Vol. 37.] 1940. [No. 6.

## SUMMARY OF RECENT ABSTRACTS.*

### V. LEISHMANIASIS.

#### A. Visceral Leishmaniasis.

*Epidemiology.*

In the epidemiology of kala azar the most important recent work strengthens the opinion that the dog is the principal reservoir of the disease. In this respect Adler *et al.* (p. 443) emphasize the importance of house dogs as well as street dogs in Canea, Crete, and Papantonakis (p. 1028) refers to the growing belief that the dog is the reservoir in that district. In Marseilles, Giraud and Bergier (p. 1026) show that kala azar in man occurs chiefly between the ages of 1 and 3 years, and that the majority of cases come from the surrounding districts or from houses in the suburbs where there are gardens. Canine kala azar is common and is found chiefly in these districts, and the authors conclude that kala azar is essentially a canine disease which passes to man accidentally. Sergent *et al.* (p. 1026) state that Mediterranean kala azar appears to be transmitted by *P. perniciosus* from dog to dog and from dog to man rather than from man to man, the dog constituting the principal reservoir. Mendes (p. 1028) found leishmania in 5 of 240 dogs examined post-mortem in Lisbon. Feng *et al.* (p. 1027) record the skin lesions found in 12 dogs with canine leishmaniasis in Peiping, and Ho (p. 1027) notes that one of these dogs came from a house in which a case of kala azar in a child occurred. The lesions in the dog appeared before those in the child. Chagas *et al.* (p. 446) in the municipality of Abialé, in the State of Pará, Brazil, where 8 cases have recently been reported, found no infection in 1,446 wild animals but among domestic animals 7 dogs and 1 cat were found to be infected. da Cunha (p. 1027) shows that in the dog experimentally infected with leishmania of S. American kala azar, the skin becomes infiltrated with macrophages containing the parasites. The skin may appear to be quite normal or may develop areas of tumefaction in which leishmania may be found.

Blanc (p. 1028) found that a squirrel (*Xerus getulus*) bred at the Pasteur Institute in Morocco had died of an acute leishmania infection,

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1939, Vol. 36. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

but the origin could not be traced. He discusses the possibility of this animal being a reservoir. In the Sudan, where visceral, oral and cutaneous infection may coexist in the same area, KIRK (p. 445) states that the visceral form, which is the most common, occurs in rural districts in the vicinity of water and in the presence of vegetation. Endemic foci in Darfur and the Blue Nile are separated by an area in which sporadic cases occur from time to time. Epidemiological evidence points to the possibility of the existence of some alternative or reservoir host.

VALLETEAU DE MOUILLAC *et al.* (p. 450) report that kala azar is becoming increasingly common in Cherbourg. ABRAMOV (p. 443) shows that kala azar is not uncommon in both children and adults in the malarious districts of Yugoslavia. SHAPIRO and BTESH (p. 1031) record 8 cases of infantile kala azar from Haifa. ARAR (p. 444) reports kala azar from Turkey, and ROBINSON (p. 445) a case in a child in Transjordan.

SCHRETZENMAYR *et al.* (p. 445) report an outbreak in Chinese troops in Canton where the disease was not previously known. The infection was probably introduced by soldiers from N. China where it is endemic. GATTI *et al.* (p. 1032) record kala azar in a patient probably infected in N. Bolivia where the disease has not previously been reported.

### *Aetiology.*

DA CUNHA (p. 447) has succeeded in infecting hamsters, monkeys and dogs with the parasite of S. American kala azar (which, though known as *L. chagasi*, cannot be differentiated from *L. infantum* or *L. donovani*) by using young cultures. As a result of a series of serological tests he (p. 447) concludes that the parasite of S. American kala azar is identical with *L. infantum*. He (p. 1027) also shows that the skin lesions of dogs infected with the leishmania of S. American kala azar resemble those of dogs infected with *L. infantum*, which is additional evidence in favour of the identity of the two species.

LWOFF (p. 447) shows that for the cultivation of *L. tropica* and *L. donovani* (as of *Trypanosoma cruzi*) three substances are essential: haematin, ascorbic acid and an unknown substance contained in serum. Haematin and ascorbic acid are contained in washed red blood cells. The leishmania will grow in peptone media to which these three ingredients are added. ZAMBRANO (p. 1024) has cultivated leishmania on NNN medium to which physiological saline or skimmed goat's milk has been added. SENEKJI (p. 1024) however, considers that ordinary NNN medium is not very satisfactory for the primary isolation of *L. tropica*. He describes an agar medium to which defibrinated rabbit blood is added, in the condensation water of which primary cultures are readily obtained. ARCHETTI (p. 448) has found Reichenow's medium to be suitable for the growth of leishmania; it consists of equal parts of citrated human blood and Ringer's solution, and is allowed to stand in the ice chest until the red cells have settled and become covered with a layer of leucocytes before inoculation with the leishmania.

GAVRILOV and LAURENCIN (p. 448) have cultivated leishmania in cultures of tissues from the embryo of the hamster made up with heparinized blood, embryonal fluid and extract of spleen. Penetration of the cells by the flagellates, development into leishmania forms and multiplication were observed.

*Transmission.*

The majority of the work done provides confirmation of the view that sandflies are the usual agents, that certain sandflies are easily infected by feeding on dogs and that the rate of infection of the sandflies is in proportion to the number of parasites available to them; but a suggestion is made that in S. France the dog tick may act as vector.

As noted above SERGENT *et al.* (p. 1026) state that Mediterranean kala azar appears to be transmitted by *Phlebotomus perniciosus* from dog to dog and from dog to man, rather than from man to man; they further show that the presence of parasites in the skin of dogs suffering from kala azar allows ready infection of the sandflies. A similar conclusion may be inferred from the work of DA CUNHA (p. 1027). In Canea, Crete, where visceral and cutaneous leishmaniasis occur in adjacent but well defined areas, ADLER *et al.* (p. 443) have shown that *P. major* is the vector of the visceral disease and *P. sergenti* that of the cutaneous form. Canine kala azar is common in the district in which human visceral leishmaniasis occurs, and the percentages of *P. major* which became infected after feeding on infected dogs in different batches varied from 2 to 70. Certain other studies on sandflies are recorded.

ADLER and THEODOR (p. 1025) obtained infection of *P. papatasi* by allowing them to feed through a membrane on emulsions of *L. chagasi* [the parasite of S. American visceral leishmaniasis which is probably identical with *L. donovani* and *L. infantum*, see above, *Aetiology*]. The percentage of flies becoming infected increases with the increase of the flagellate content of the emulsion and may rise to 89 per cent. When infection has been established the flagellates multiply in the midgut and ascend to the anterior part of the cardia which may become choked with them. Passage to the oesophagus may occur as early as three days after feeding.

FERREIRA *et al.* (p. 449) showed that the parasite of S. American kala azar was able to develop in wild *P. intermedius* which had fed on infected dogs. The sandflies occur in and around the houses of the patients, and breeding places have been found near the houses. The authors failed to obtain infection of laboratory bred *P. intermedius* fed on dogs, but CHAGAS (p. 449) later reports success in this way with laboratory bred *P. intermedius* and *P. longipalpis*.

FENG and CHUNG (p. 1025) found that infection occurred in both *P. sergenti* var. *mongolensis* and *P. chinensis* when fed on infected dogs, but that the infection persisted only in *P. chinensis*, in which it extended forwards to the pharynx and proboscis. Flagellates were found in the faeces of one *P. chinensis*. The rate of infection was proportional to the degree of infection of the skin of the dogs. *P. chinensis* is therefore a satisfactory host for the parasite of canine kala azar and if this parasite is identical with that of human kala azar this finding may throw light on the epidemiology of the human disease, and supports the conclusions previously arrived at by HINDLE and other workers that in N. China it is the vector concerned in man. CHUNG and FENG (p. 1025) found flagellates indistinguishable from developing leishmania in *P. chinensis* from the kennel of a dog suffering from kala azar and the house of its owner in Peiping.

GIRAUD and BERGIER (p. 1026) in Marseilles suspect the dog tick of transmission of kala azar from dogs to children. The disease in children

is common in those districts in which dogs are infected ; the ticks bite children playing on the ground and children are more closely in contact with dogs than are adults (in whom kala azar is rarely found) ; sandflies on the other hand bite children and adults impartially, but dogs less often. The authors mention one child who suffered from boutonneuse fever followed two months later by kala azar, and surmise that both infections may have been acquired at the same time by the same means.

ROBINSON (p. 445) found *P. papatasi* and *P. major* in Transjordan where he has found kala azar. *P. major* is probably the vector. KIRK (p. 445) in the Sudan shows that so far as is known, *P. langeroni* is the only sandfly which bears any relation in its distribution with that of leishmaniasis. CHAGAS *et al.* (p. 446) found *P. longipalpis* in a district of Brazil in which kala azar was present.

### *Pathology.*

MENON (p. 1029) regards kala azar as a reticulo-endotheliosis caused by parasitic invasion of the cytoplasmic reticular syncytium with gradual formation of free parasitized histiocytes and, in the later stages, spread of infection to the lymphatic reticulum of the spleen. Reticulo-endothelial blockage is the probable cause of the anaemia and of the tendency to inflammatory complications. MURANO and VECCHIO (p. 1029) consider that the anaemia is due to hyperplasia of bone marrow caused by alterations in the reticulo-endothelial system brought about by the leishmania, and not to any haemolytic process.

In dogs ADLER *et al.* (p. 443) describe an infiltration of the vocal chords with infected macrophages, which probably explains the inability of some of the animals to bark.

KRISHNAN (p. 449) states that although normal human serum and serum from patients with kala azar have *in vitro* a lytic action on cultural forms of *L. donovani*, their presence *in vivo* does not help in bringing about cure.

### *Clinical.*

CHUNG (p. 450) regards sternal puncture as the best method for diagnosing kala azar, and describes the use of a shortened lumbar puncture needle for the purpose. NAPIER (p. 1030), however, though admitting that sternal puncture is a fairly accurate means of diagnosis, concludes that it has not been proved to be as reliable as splenic puncture which in his hands has not given rise to any serious effects.

Discussing the formol-gel reaction DE VRIES (p. 1029) has found it positive, in many different diseases, whenever the total globulin content reaches 37 parts per thousand or more. It is not specific. DA CUNHA and DIAS (pp. 451, 1035) have prepared a leishmania antigen which gives very definite complement-fixation reactions with sera from man or animals suffering from both visceral and cutaneous leishmaniasis. GREVAL *et al.* (p. 1030) write of the high diagnostic value of the Witebsky-Klingenstein-Kuhn reaction, which was positive in every one of 132 diagnosed cases.

PALLISTER (p. 1030) records an incubation period of one to two years in kala azar.

SCHRETZENMAYR *et al.* (p. 445) report that jaundice was a feature in their cases in Canton, and that in one there developed acute atrophy of the liver.

VALLETEAU DE MOUILLAC *et al.* (p. 450) observed symptoms of meningitis with purulent cerebrospinal fluid in a child suffering from kala azar in Cherbourg. The fluid was bacteriologically sterile and they conclude therefore that the condition, which cleared up, was due to kala azar. One injection of 20 cc. antimeningococcus serum had been given as a precaution.

DASTIDAR (p. 1031) reports a nodule on the tongue, in which leishmania were found, in a case of post-kala azar dermal leishmaniasis.

*Treatment.*

Working with normal and infected hamsters, WANG (p. 452) finds that solustibosan, neostibosan and ureastibamine are increasingly toxic with regard to the amount of antimony which can be administered, and are increasingly potent in cure, in that order. He (p. 1032) shows that daily injections appear to be less effective than bi-weekly or tri-weekly injections, probably due to the fact that when the antimony in the tissues reaches a certain level excretion by the kidneys becomes suddenly increased out of all proportion to the antimony in the tissues.

D'OELSNITZ *et al.* (p. 451) give the highest tolerated doses of antimony continued over a long period. In the case of ureastibamine, 0·5 cgm. per kilo. body weight can be given daily until a total of over 0·5 gm. per kilo. has been administered, and with other organic antimonials this may be exceeded, but careful watch must be kept for signs of intolerance. In one female patient 0·5 gm. neostibosan was given almost daily for 2½ months until a total of 34 gm. had been given.

AVERSA (p. 1033) obtained good results in infants with solustibosan. MIRZOJAN (p. 1033) writes in favour of sourmine (stibosan) in Russia. DAS GUPTA (p. 1033) reports two cases of urticaria (with unconsciousness in one and uterine haemorrhage in the other) after ureastibamine.

MATHIESON and WATSON (p. 452) record successful treatment with neostam after the failure of fouadin in one patient.

*Control.*

SERGENT *et al.* (p. 1026) show that a reduction in the human reservoir of Mediterranean kala azar by treatment of all cases has not been followed by a lowered incidence of the disease. On the assumption that the dog is the principal reservoir they therefore suggest the destruction of all known infected dogs and all stray dogs, the control of the movement of dogs into and out of infected areas, the prevention of contact between children and dogs, and measures for the protection against sandfly bites by nets and other means. Breeding of sandflies can to some extent be prevented by general cleanliness. PAPANTONAKIS (p. 1028) shows that the destruction of the majority of the dogs in Canea in 1933 was followed by a markedly lower incidence of human kala azar in the following year. Regulations have now been drawn up insisting on inspection of all dogs in April of each year, when the formol-gel tests and clinical examination are made. All positive or sick dogs are destroyed and if in a village a human case occurs, all dogs of the village are destroyed or tested and the residents can only obtain new dogs which are under two months of age and which have come from uninfected villages. ADLER *et al.* (p. 443) emphasize that in any campaign of dog destruction both house and street dogs must be taken into account.

## B. Cutaneous Leishmaniasis.

### *Epidemiology.*

Esnault and Loubet (p. 453) found a case in S. Algeria in a district in which it has been unknown for 12 years. It appears that for some unexplained reason the disease occurs in small outbreaks separated by long intervals of time. Vanni (p. 453) reports 300 cases of oriental sore found in two months in the Province of Abruzzi, chiefly in the coastal rural districts, and Poggi and Monti (p. 1033) record the incidence in further valleys of the Province of Forli.

Pifano (p. 1035) reports 36 cases in the State of Yaracuy in the Argentine. The majority had cutaneous lesions only, some were mixed, and in two there were mucosal lesions only.

### *Aetiology and Transmission.*

Higoumenakis (p. 453) discusses the relationship of oriental sore to kala azar and concludes that the parasite of oriental sore in endemic foci is probably that of kala azar which has decreased in virulence through many skin passages and has thus ceased to produce generalized infections. The parasites of sporadic infections, however, retain much of their virulence and can produce visceral infections in experimental animals.

Weinman (p. 1036) describes a procedure by which tissue invading leishmania forms of *L. tropica* may be obtained in culture from the flagellate forms. Pieces of guineapig lung or spleen are bathed in a rich culture of flagellates and placed on NNN blood agar or Zinsser's serum-Tyrode agar; the cells of the tissue survive for 11 days or more at 37°C. and the leptomonads live in the fluid which collects round each piece of tissue, while in the tissue typical leishmania forms appear and multiply.

Vanni (pp. 453, 1034) records evidence that *P. macedonicus* is the vector in Abruzzi. Jerace (p. 1034) shows that in the Province of Teramo the distribution of *P. perfiliewi* coincides with that of cutaneous leishmaniasis. Adler *et al.* (p. 443) show that in Canea *P. sergenti* is the vector of cutaneous leishmaniasis.

Berberian (p. 1034) has now made four successful mechanical transmissions of oriental sore by means of *Stomoxys calcitrans*.

### *Clinical and Treatment.*

Berberian (p. 1035) has produced sores by the inoculation of cultures of *L. tropica* into volunteers and considers that in this way immunity against the development of oriental sore on exposed parts of the body may be conferred. Inoculation of cultures into immune persons is followed by definite skin reactions, both immediate and delayed.

Higoumenakis (p. 453) describes oriental sores of unusual type in Greece; the lesions were multiple and of long duration, and in one child skin lesions resembling oriental sore appeared during the course of kala azar. These he regards as cutaneous manifestations of the generalized infection.

Porte (p. 454) uses intravenous neostibosan successfully in treatment, whereas local treatment has not been useful. Flarer (p. 454) injects 0·05 to 0·1 gm. atebrin, dissolved in 1·0 or 2·0 cc. distilled water into the skin around the sores, with rapidly successful results. The dose may be increased to 0·3 gm. Castellani and Amalfitano

(p. 454) have used a fuchsin paint in three cases, obtaining cure in two to three and a half months.

REYES ORIBE (p. 455) has obtained good results with fouadin combined with intravenous yatren in S. American muco-cutaneous leishmaniasis, and PIFANO (p. 1035) considers intramuscular fouadin to be the treatment of choice for this condition. *C. Wilcocks.*

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## TRYPANOSOMIASIS.

### *PRÉCIS* OF ABSTRACTS IN THIS SECTION.

KAUNTZE (p. 397) reports on sleeping sickness in Uganda during 1938. SAUNDERS (p. 397) reports incidence varying from 3 to 9 per cent. in the Gold Coast ; it is decreasing in one area apparently as a result of clearings. VAN HOOF (p. 397) shows that in the Congo over 5 million persons were examined in 1938. The index of new infection has fallen during the last 10 years from over 1·0 per cent. to about 0·27 per cent. DE BRAUWERE (p. 398) reports on the trypanosomiasis campaign of Foréami, quoting a case regarded as hereditary infection. He discusses arsenic resistance and ocular sequelae of treatment and points out the value of rural dispensaries in the treatment of natives in their own villages.

ACANFORA (p. 399) discusses the nomenclature of the trypanosomes.

ROUBAUD and PROVOST (p. 399) induced in a cock an infection with *T. rhodesiense.* No symptoms were produced and infection could only be demonstrated by animal inoculation.

JACK (p. 400) reports observations on the behaviour of *G. morsitans*, which is apparently attracted to animals by movement, scent and shade. Its reaction to stimuli is determined largely by the state of nutrition, water content and pregnancy. The details given in the abstract cannot further be summarized.

LAVIER and LEROUX (p. 401) describe the pathological appearances of the heart in human trypanosomiasis, emphasizing the intense myocardial sclerosis.

ROBIN and BROCHEN (p. 402), after comparative tests, consider that, though sternal puncture has some value in *T. gambiense* infections, it is not so good as gland juice or blood examination. CROZAFON (p. 402) prefers direct examination of fresh gland juice to the other methods of diagnosis. GEORGIADÈS (p. 402) shows that in 3 of 11 cases there appeared to be a significant increase in lymphocytes in the cerebrospinal fluid as a result of lumbar puncture.

SALEUN (p. 403) reports on trypanosomiasis in French Equatorial Africa and discusses possible causes of failure of drug cure.

LOURIE and YORKE (p. 404) record the very high trypanocidal power of certain aromatic diamidines in mice infected with a laboratory strain of *T. rhodesiense*, giving details of chemical formulae. There was no action in *T. cruzi* or certain spirochaetal infections. The same authors (p. 405) show that certain of these compounds are very active against *Babesia canis* infections of puppies, but that *B. canis* can readily be made drug-resistant.

DE BORCHGRAVE (p. 406) shows that argoflavine and atebrin may remove *in vitro* the infecting power of *T. gambiense* and that the action of argoflavine is enhanced by strong light.

COON and ELLIS (p. 406) each describe the symptoms of nitritoid reactions after injections of tryparsamide. In each case the reactions occurred not after the first injection but when a considerable number had been given.

*Trypanosomiasis of animals.*—CULBERTSON and WOTTON (p. 407) found that ablastin is produced well in rats aged 25 days or more and infected with *T. lewisi*, but that in younger animals production is poor. They conclude that the power of producing ablastin is a major factor in the resistance shown by older rats, which usually survive the infection. KOLODNY (p. 408) reports similar findings and conclusions in rats infected with *T. cruzi*. CULBERTSON (p. 409) shows that, as with rats infected with *T. lewisi* and *T. cruzi*, immunity to subsequent infection is transmitted in the colostrum and milk from mice infected with *T. duttoni*, or passively immunized, to their young. The immunity is specific.

ACANFORA (p. 409) has demonstrated multiplication of *T. brucei* in the blood of fowl embryo. BIOCCA (p. 410) used an emulsion of infected fowl embryo to vaccinate guineapigs against *T. brucei* and found that this procedure prolonged the course of the disease. VAN DEN BRANDEN (p. 410) found that rabbits infected with *T. brucei* gave positive complement fixation tests with an antigen of alcoholic extract of *T. brucei*, whereas normal animals did not.

DUBOIS and KOHN (p. 410) discuss the action of arsenobenzol on *T. brucei* and quote experiments which favour the view that it is direct, but they do not exclude the possibility that 914 acts by virtue of transformation into arsenoxide. DUBOIS and LOSNER (p. 411) show that blockage of the reticulo-endothelial system does not appear to produce any constant change in the elimination of 914 in animals.

RICHET and ANTOINE (p. 412) report that considerable immunity to reinfection is afforded to rats infected with *T. equiperdum* and given a curative dose of sulpharsenol during the course of infection.

KRANEVELD and UMBOH (p. 412) show that the therapeutic effect of naganol in guineapigs infected with *T. evansi* is lessened if the drug is given in fractional doses with a day's interval between injections.

*Chagas's Disease.*—MAZZA (p. 413) reports on the incidence of Chagas's disease in the Argentine and names the animals found naturally infected and the insect vectors principally concerned.

ROUBAUD and ROMAÑA (p. 413) have shown that *T. cruzi* can survive in fowl embryo for a week, but have not demonstrated multiplication.

GASIC (p. 414) found infection in half of a series of *T. infestans* examined in the province of Coquimbo, Chile. HOFFMANN (p. 414) shows that in Cuba *T. flavida* experimentally can transmit *T. cruzi* and points out the risk of the admission of patients with Chagas's disease.

MAZZA *et al.* (p. 414) describe the pathological changes in the heart in a case of chronic disease, and MAZZA and JÖRG (p. 415) compare the cardiac lesions with those of rheumatism. The changes in the heart observed on radiological examination are discussed by ALBERTO AGUIRRE and GIMENEZ (p. 415). MAZZA (p. 415) describes a nodular hepatitis which he regards of diagnostic importance in Chagas's disease and suggests that examination of liver and heart tissue removed post-mortem by the viscerotome may be valuable in epidemiological studies. ROMAÑA (p. 416) describes the histological changes in the organs and in the eye of a monkey infected with *T. cruzi* by deposition of infected faeces of *R. prolixus* on the conjunctiva.

LEITE (p. 416) concludes from the results of a series of Machado-Guerreiro complement fixation tests in goitrous patients in Brazil that goitre is not an essential part of the picture of Chagas's disease.

*C. W.*

UGANDA PROTECTORATE, ANNUAL REPORT OF THE MEDICAL DEPARTMENT FOR THE YEAR ENDED 31ST DECEMBER, 1938 [KAUNTZE (W. H.), Director].—[**Trypanosomiasis** pp. 38–39.]

The Victoria Nyanza area remained free of sleeping sickness, but clearings have been maintained and the rules enforced to prevent the disease from being introduced from other areas. No cases have been reported from the Lake Edward-George area, notwithstanding the development of the fishing industry. In Gulu six-monthly inspections were made of the newly-settled areas at Anaka, Nwoza and Alero. Four new cases were diagnosed and six old cases treated. No new cases were discovered in Madi. In the West Nile area there were 684 cases in 1938, compared with 728 in 1937. An entomological survey was made at the end of the year, and the recommendations of Mr. E. G. GIBBINS, who made the survey, are recorded.

*W. Yorke.*

SAUNDERS (G.). **Trypanosomiasis Campaign—Progress Report.**—*Gold Coast Rep. Med. Dept. Year 1938.* Appendix V. pp. 104–107.

Details are given regarding the infection rates in the various sleeping sickness areas in the northern territories. In the Lawra area the information at present is unreliable ; in the Burifoo area the average infection rate is 3 per cent. ; in Nadawli it is 9 per cent. ; in the border area between Lawra and Tumu it is 6 per cent. ; whilst in South Mamprussi and Kusasi it is 1 per cent. The number of patients treated in the field was 98 in Lawra-Tumu, 95 in Wa district and 333 in Mamprussi.

A considerable number of cases who were positive last year were found to be still positive this year, and have had no symptoms nor treatment in the interval. This apparently applies to 20 per cent. of last year's positive cases. At one town three miles from Gambaga the figure was 50 per cent. (5 out of 10 cases).

The incidence of the disease is decreasing in Mamprussi ; the decrease appears to be due mainly to the clearings.

A certain amount of information is given regarding a topographical study of incidence, hospitals and dispensaries, and public health measures.

*W. Y.*

CONGO BELGE : RAPPORT SUR L'HYGIÈNE PUBLIQUE AU CONGO BELGE PENDANT L'ANNÉE 1938 [VAN HOOF (L.)].—[**Trypanosomiasis** pp. 33–49. With 1 folding map.]

Eleven Europeans suffering from sleeping sickness—ten from the province of Leopoldville and one from Coquilhatville—have been treated during the year.

The personnel of the medical service was only completed towards the end of the year 1938, and consequently it was not possible to extend the sleeping sickness work amongst the natives. The regions

most heavily infected have received greater attention than formerly, and the precision of diagnosis has been improved by the general adoption of the most practical methods, the improvement of scientific material and the training of good native microscopists.

As regards treatment, success has been obtained in a high proportion of cases, and this fact is now recognized by the natives, who do not hesitate to present themselves willingly for examination and treatment. As a result, there is a considerable increase in the number of cases treated in hospitals and in rural dispensaries.

A table is given, showing the number of cases examined during each of the last 12 years, the number of old cases of sleeping sickness under control, the number of new cases discovered, and the index of new infection. In 1927, the number of cases examined was 1,704,477. This number has steadily risen year by year, until in 1938 it was no less than 5,034,331. In this year the number of old cases under control was 45,785 and the number of new cases found was 13,454. The index of new infection has fallen during the last ten years from over 1 per cent. to about 0·27 per cent.

The report consists almost entirely of figures showing the state of affairs as regards sleeping sickness in the various areas into which the Belgian Congo is divided. It is impossible to summarize these figures, and those interested must consult the report in the original. *W. Y.*

CONGO BELGE: FONDS REINE ELISABETH POUR L'ASSISTANCE MÉDICALE AUX INDIGÈNES DU CONGO BELGE. RAPPORT ANNUEL 1938 [DE BRAUWERE, Médecin-Directeur]. pp. 44–63. With 1 map.—A.—Maladie du sommeil. [**Sleeping Sickness.**]

The report opens with some remarks on diagnosis. Gland palpation and clinical examination are the procedures of choice, and these are followed by gland puncture. Blood examination is not practised systematically, but is reserved for suspected cases in whom gland puncture fails to reveal trypanosomes. Various observers have, however, found that in certain areas a single gland puncture revealed trypanosomes in definitely fewer cases than did examination of a stained thick blood preparation.

Details are given of infection in a child aged 10 days, whose mother was also infected; the child had an enlarged liver and spleen, was very cachectic, and died 3 months after birth. It is suggested that this was a case of hereditary infection. In the same place, multiple infections in the same family were common.

Systematic investigation has shown that arsenic-resistance is more common than was formerly thought. The physician-in-chief has recommended a simple and practical method which enables one to affirm with a high degree of probability that trypanosomes are arsenic-resistant. This method [the nature of which is not disclosed] revealed 39 cases in 9 different districts; in addition, a certain number of suspects were encountered in each of these districts and some also in other places. Although resistant cases were discovered in 9 places, only 3 of them can be regarded as foci of arsenic-resistant cases; in the remainder the resistant cases were sporadic. Isolated cases of apparent arsenic-resistance may be only a therapeutic incident, and their real nature can be determined only by animal inoculation and tests, but the discovery of a number of resistant cases in the same focus

imposes the diagnosis of a resistant strain. The treatment of arsenic-resistant cases continues as heretofore to be Belganyl (Bayer 205) and antimonials, either together or alternately; the results are satisfactory.

Ocular troubles resulting from treatment are becoming more and more rare. The tryponarsyl is always employed fresh and the water in which it is dissolved is always distilled. The gravity of this regrettable complication depends in large measure on the degree of intelligence of the patient, who is always questioned strictly about his sight during a course of treatment. Amongst 8,393 cases of sleeping sickness treated during the year, 21 exhibited visual disturbance; in 13 of these the trouble was slight and disappeared entirely, in 4 it was ameliorated, but in 4 it persisted.

Thanks to the equipment of a very large number of rural dispensaries, the sick have been treated in their villages. This is greatly preferred by the natives, and the success of treatment is largely due to this fact.

The number of people examined during 1938 was 898,333, and of these 2,548 (0·28 per cent.) were found to be infected with trypanosomes. The total number treated was 8,393 and the death rate was 4·54 per cent. In all, 3,292 lumbar punctures were performed—2,704 in those in whom trypanosomes had been found and 588 in suspected cases. Details are given. The article closes with statistics regarding the state of affairs in the various sleeping sickness districts.

*W. Y.*

ACANFORA (Giuseppe). Sul tripanosoma rotatorium. [*T. rotatorium.*]—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1939. Dec. Vol. 20. No. 12. pp. 625–636. With 8 figs.

Examining the blood of a number of frogs captured in the vicinity of Rome the author has encountered the common trypanosome of these animals. He has noted the extreme polymorphism of this parasite and is convinced that the genus *Trypanosoma* founded for this organism should not include the more uniform trypanosomes of warm-blooded animals, for which the genus *Castellanella* of CHALMERS may be employed [but see this *Bulletin*, 1938, Vol. 35, pp. 327, 328].

*C. M. Wenyon.*

ROUBAUD (E.) & PROVOST (A.). Infection inapparente de la poule par *Trypanosoma rhodesiense.* [**Unapparent Infection of the Fowl with** *T. rhodesiense.*]—*Bull. Soc. Path. Exot.* 1939. Oct. 11. Vol. 32. No. 8. pp. 807–809.

Farmyard birds appear to be irregularly susceptible to infection with the trypanosomes of man and stock. The authors briefly summarize the observations of previous workers in support of this statement. They refer amongst others to the numerous observations of MESNIL, LEGER and PERARD (1928–1935) who used various strains, especially *T. rhodesiense*, in attempts to infect a large number of fowls of different ages; the results were always negative.

The authors then record a couple of experiments made by them with Mesnil's strain of *T. rhodesiense.* Two fowls were inoculated into the caruncle. One of them, a hen, did not become infected, but the other, a cock, developed a latent infection. Trypanosomes were never

discovered in the blood by microscopical examination, but their presence was demonstrated for more than a month by inoculation into mice. The cock, which was suffering from a chronic infection of *Plasmodium gallinaceum*, exhibited no signs of the trypanosomal infection.

*W. Y.*

JACK (R. W.). **Studies in the Physiology and Behaviour of** *Glossina morsitans* **Westw.**—*Mem. Dep. Agric. S. Rhodesia.* 1939. No. 1. pp. 4+203+vii. With 3 plates & 27 figs. [37 refs.] [Summarized in *Rev. Applied Entom.* Ser. B. 1940. Feb. Vol. 28. Pt. 2. pp. 22–24.]

"This paper, which is divided into two parts dealing respectively with the physiology and behaviour of *Glossina morsitans*, Westw., is based on the results of laboratory research carried out at Salisbury, Southern Rhodesia, since 1936 and on certain data, referring chiefly to behaviour, collected in the field over a number of years. A short section of the first part deals with high and low fatal temperatures and factors that may influence their variation, and with the effect of insolation. The rest of the part is chiefly concerned with the influence of atmospheric conditions on the pupae and adults, but includes such questions as the water and fat contents of the flies on emergence, the processes following feeding, the influence of pregnancy on water and fat contents, and the stimulus to feeding.

"The subjects dealt with in the second part include the reactions of the flies to light, temperature, humidity, etc., the attraction of flies in the field to man, animals, motor vehicles, screens, colours, and traps, the elementary positive reactions, such as those to movement, scent and shade, on which attraction depends, and finally, a discussion of the 'feeding ground concept.'

"The following points are taken largely from the part of the author's summary that deals with the attraction of flies in the field: There is as yet no evidence of attraction to man other than through the external stimuli of movement or scent. Males are attracted whether hungry or not, but females only when very hungry. As regular feeding is necessary for normal reproduction, it follows that man cannot take the place of animals as a host of *G. morsitans*. Most flies that attack a stationary animal do so under the belly, usually well back, and it is suggested that they are primarily attracted by the patch of shade presented. Females with a fat content higher than those that are attracted to man may be attracted to a donkey. Flies are apparently attracted to animals by movement, scent and shade. Over the same route, more flies are attracted to a motor vehicle than to man, and although the percentage of females is no higher, their mean fat content is much greater. A moving lorry apparently attracts females that are ready to feed in spite of a considerable fat content, whereas man attracts only more or less starving females.

"Dark colours are markedly more attractive than light ones, at least in the dry season, and this preference is noticeable in the case of both screens and moving natives. A dark blue screen was considerably more attractive than a live donkey. Screens of either black or hessian cloth attract a higher percentage of females than a man or lorry, but black attracts a higher percentage than hessian. The shady side of a black screen attracts more flies and a higher proportion of the fatter females than the sunny side, at least in very hot, dry weather. Various types of traps were tested, including some designed expressly to attract flies into dark shade. Flies entered the traps when the opening was on the shady side quite as readily as when it was underneath, and in the case of one model penetrated into the very dark interior through a slit ¼-inch wide. The percentage of females among flies caught in traps in the dry season was greater than among those caught on man or on a vehicle, and in certain

instances slightly exceeded 50. A few figures obtained in the wet season indicated that the percentages in traps and on man are then similar. There is an indication that the strong preference for dark blue or black may be exhibited only under dry season conditions, since a few tests during the rains suggest a preference for hessian. Catches in the traps, which were negligible during the rains and very low during the cooler part of the dry season, rose during August and remained fairly high during September, and part of October but became negligible again after the first heavy rains. The dominant factor determining the reaction to traps appears to be evaporation rate, since the temperature rises as high in the wet season as in August. The falling off of catches in October may be due to the fact that the flies are inactive during the greater part of many very hot days. Restriction of shade in the late dry season is probably a factor contributing to the increased catches at this time. The nature of the attraction exercised by the Harris trap and other somewhat similar models is discussed, and it is thought more likely that the flies are attracted by the patch of shade, or what looks like shade, than that they mistake the trap for an animal; hunger is not apparently the primary stimulus. The reaction of a fly to stimuli (moving objects, scent, shade and, questionably, bulky objects) is determined largely by its physiological condition, namely, state of nutrition, water content and pregnancy.

"Hungry flies are attracted to the better illuminated spots in the forest because hunger increases activity and the positive reaction to light. After feeding, the flies usually return to shade, chiefly for the processes of primary excretion and concentration of the ingested blood, but actual resting after a meal occupies a few hours at most. Female flies are presumably attracted to shady retreats for larviposition, but this is a rapid process. Active flies normally range continuously through their habitat, and activity is not confined to hungry flies. A forest opening or vlei, if evergreen trees are present, and pure mopane (*Copaifera mopane*) forest, when in leaf, are commonly complete habitats for the fly. It appears that the applicability of the feeding ground concept, even in the modified form indicated, depends greatly upon the physical conditions presented by the local forest."

GHIDINI (Gian Maria). Nuovi dati sulla distribuzione delle Glossine nelle terre dell'Impero. [**The Distribution of Glossina in Italian East Africa.**]—*Riv. di Biol. Colon.* Rome. 1939. Oct. Vol. 2. No. 5. pp. 329–333. With 2 figs. English summary (3 lines).

"The author records the presence of *Gl. tachinoides, palpalis, fuscipes* and *pallidipes* in the district of Gambela on the confines of the Italian East Africa with the Anglo-Egyptian Sudan."

LAVIER (G.) & LEROUX (R.). Lésions cardiaques dans la maladie du sommeil. [**Cardiac Lesions in Sleeping Sickness.**]—*Bull. Soc. Path. Exot.* 1939. Dec. 13. Vol. 32. No. 10. pp. 927–929. With 1 plate.

Notwithstanding the studies of LOW and CASTELLANI, of MOTT, of THOMAS and BREINL, and the more recent work of PERRUZZI on experimentally infected monkeys, the lesions of the heart in sleeping sickness have not received the attention they merit. The authors have examined carefully sections of small pieces of cardiac tissue from two cases of sleeping sickness sent to them from the Belgian Congo.

Both cases showed typical and very pronounced epicarditis, sclerotic endocarditis and periarterial myocarditis with arteritis of the branches of the coronary vessels. These changes are comparable with, but much more pronounced than, those found by Perruzzi in his infected monkeys. The fact that the lesions, especially the intense myocardial

sclerosis, found by the authors were more pronounced than those observed by Perruzzi is explained on the ground that the disease evolved much more slowly in the human cases. The authors consider that the lesions were so intense that the physiological function of the heart must have been seriously disturbed. *W. Y.*

ROBIN (Ch.) & BROCHEN (L.). Le diagnostic de la trypanosomiase humaine par ponction de la moelle osseuse. Résultats et déductions pratiques de 60 ponctions sternales. [**Diagnosis of Human Trypanosomiasis by Bone-Marrow Puncture.**]—*Bull. Soc. Path. Exot.* 1939. Oct. 11. Vol. 32. No. 8. pp. 830–835.

Reference is made to the fact that Robin and JOSPIN [this *Bulletin*, 1937, Vol. 34, p. 928] had found that *T. gambiense* was constantly present in the bone-marrow of infected guineapigs. They have now examined the point in human beings in various stages of sleeping sickness. The results of their observations are given in tables: Table 1 gives the result of examination of the gland juice, the spinal fluid and the bone-marrow in 9 early cases with normal spinal fluid; Table 2 gives similar data in 13 cases with meningeal reaction (slightly changed spinal fluid); and Table 3, the same in 28 late cases (with profound changes in the spinal fluid).

The general conclusions drawn are that, although the technique of sternal puncture is simple and painless and can be practised in the bush, yet its indications are limited because examination of the gland juice and blood gives a greater proportion of positive results than does bone-marrow puncture [*vide* also GUIBERT, this *Bulletin*, 1938, Vol. 35, p. 704]. *W. Y.*

CROZAFON (Charles). Le dépistage des trypanosomés en équipe de prospection. L'examen du sac ganglionnaire: état frais et suc coloré. [**The Search for Cases of Sleeping Sickness by Travelling Missions. The Examination of Fresh and Stained Specimens of Gland Juice.**]—*Ann. de Méd. et de Pharm. Colon.* 1939. July–Aug.–Sept. Vol. 37. No. 3. pp. 742–746.

In a recent paper, RAOULT has advocated the examination of stained smears of gland juice as a means of diagnosing trypanosomiasis in the bush [this *Bulletin*, 1938, Vol. 35, p. 703]. The author has examined the method in the same sleeping sickness district as that in which Raoult worked, and abandoned it. He considers that the examination of fresh specimens of gland juice is, apart from that of triple centrifugation of blood, the best method of diagnosis. Examination of stained smears of gland juice has no advantages over the above procedure, and merely adds to the labour of diagnosis and retards the work of the mission. *W. Y.*

GEORGIADÈS (D.). Contribution à l'étude de possibilités d'infection des méninges ou aggravation de la lymphocytose au cours des ponctions lombaires. [**Contribution to the Study of the Possibility of infecting the Meninges or of aggravating the Lymphocytosis by Lumbar Puncture.**]—*Ann. Soc. Belge de Méd. Trop.* 1939. Dec. 31. Vol. 19. No. 4. pp. 533–537.

The author set himself to inquire: (1) whether the irritation of the meninges provoked by the introduction of the needle during lumbar

puncture caused an increase in the lymphocytosis, or in the amount of globulin, or of both; (2) whether the haemorrhage resulting from damage to a vessel caused meningeal irritation or aggravated the condition; and (3) whether trypanosomal invasion was possible or even frequent.

The small number of observations made does not warrant conclusions. The patients were not sterilized with moranyl before puncture, because this would invalidate the experiment, at least in so far as the question of penetration of trypanosomes into the spinal fluid was concerned. The patients were allowed to rest 1 to 3 hours in the sun before puncture; none of them was seriously verminous or suffered from grave dermatitis, and all were free from yaws and syphilis.

Details are given of 11 cases. Seven of these appeared to show that notwithstanding 2 or 3 lumbar punctures performed at short intervals, a fatiguing journey, exposure to the sun, and penetration of blood into the meninges, the lymphocytosis and globulin content of the spinal fluid did not vary. On the contrary, however, 4 cases showed an increase in the lymphocytosis; in one case the number of lymphocytes increased within 48 hours from 75 to 90. In 3 cases there seemed to be a significant increase in the lymphocytosis after the first puncture, *viz.*, 4 to 12, 4 to 10, and 1·5 to 30. *W. Y.*

BRAZZAVILLE: AFRIQUE EQUATORIALE FRANÇAISE. RAPPORT SUR LE FONCTIONNEMENT DE L'INSTITUT PASTEUR DE BRAZZAVILLE PENDANT L'ANNÉE 1938 [SALEUN (G.)]. pp. 69–83.—Service de la surveillance de la maladie du sommeil. [**Sleeping Sickness Service.**]

During the year, 624 European officials and 122 non-officials were examined, but no instance of infection with trypanosomiasis was discovered; this is the first occasion on which the Brazzaville Pasteur Institute has not been called upon to treat a new European case of sleeping sickness during an entire year. Six old European cases have been kept under observation; in all the examinations of blood and spinal fluid were negative.

Among the natives, 164 new cases have been discovered and 967 old cases have been kept under observation. The methods of diagnosis employed were: gland palpation and examination of gland juice; examination of fresh coverslip preparations of blood and after triple centrifugation; lumbar puncture; and the formol-gel reaction. The results obtained from these various methods are shown in a table. It is noteworthy that in no fewer than 43 of the 164 cases diagnosis (discovery of trypanosomes) was made by lumbar puncture, the other methods giving negative results. Of the 164 new cases, 48 were in the early (blood-gland) stage, and 116 showed changes in the cerebrospinal fluid.

Of the 44 patients in the early stage, 41 have apparently been cured, but 3 relapsed. Of 99 advanced patients, 58 have done excellently in that the spinal fluid became normal; in 37 the spinal fluid had improved three months after treatment, but had not become normal; and in 4, trypanosomes were still present in the peripheral circulation and the spinal fluid had not improved. In all, 16 of the 164 new cases have died during the year. Two were moribund when discovered and died before treatment; two first-stage cases died of intercurrent disease, eight advanced cases died during treatment; two advanced

cases seemed to improve, but the disease subsequently developed rapidly and death resulted; one advanced case was uninfluenced by treatment; and one early case, a child of 12 years, died suddenly from an unknown cause after the second injection.

Details are then given of 16 old cases which died during 1938. The paper closes with a short discussion regarding the possible causes of the failure to cure in certain cases. Among these it is considered that the following play a part:—

1. Drug-resistance of the parasite; this cannot be ignored, but it is thought to account for failure to cure in only a very small number of patients.

2. Site of the anatomical lesions; the parasite may be buried in situations (bone-marrow, internal organs, and especially in the nervous system) difficult of access to the medicament.

3. Deficient defensive power of the body, resulting from social conditions, poor food and intercurrent conditions.

4. The non-utilization of the medicament. By this the author apparently means the inability of the host to transform the medicament into a more highly trypanocidal substance. [Little or nothing is known of this matter beyond the conversion of the inert pentavalent aromatic arsenicals into the powerfully trypanocidal trivalent compounds.]

5. A number of minor factors, which in themselves may appear trifling but in the aggregate may be important. *W. Y.*

LOURIE (E. M.) & YORKE (Warrington). **Studies in Chemotherapy. XXI.—The Trypanocidal Action of Certain Aromatic Diamidines.**—*Ann. Trop. Med. & Parasit.* 1939. Dec. 30. Vol. 33. Nos. 3 & 4. pp. 289–304.

In collaboration with Dr. EWINS, of Messrs. May and Baker, the authors have continued their investigations on the trypanocidal action of the diamidines. The present paper records the results of examination of a long series of aromatic diamidines prepared by Dr. Ewins. The authors summarize their results as follows:—

"In previous papers it was shown that certain guanidines, isothioureas, amidines and amines with alkyl and alkylene chains exhibited considerable trypanocidal activity. As it seemed possible that the carbon chain merely served as a carrier of the active terminal groups of strong basic nature, a number of aromatic amidine and guanidine compounds were prepared; they also were found to exhibit trypanocidal action.

"Dr. Ewins, of Messrs. May and Baker, Ltd., with the object of developing this line of investigation, prepared a large number of aromatic compounds containing the amidine group, and preliminary tests on mice showed that many of these compounds were powerfully trypanocidal.

"The present investigation is concerned with a more extensive examination of the most active of these compounds. The most important, from the trypanocidal point of view, were members of the series 4 : 4′-R-O $(CH_2)_n$O–R, where R is $\begin{matrix} NH \\ NH_2 \end{matrix}\!\!>\!C\!\langle\!\!\bigcirc$, and 4 : 4′-R-CH : CH-R. Certain members of the series 4 : 4′-R-O$(CH_2)_n$O-R, notably R-O$(CH_2)_3$O-R (diamidino diphenoxy pentane) and R-O$(CH_2)_3$O-R (diamidino diphenoxy propane), and 4 : 4′-R-CH : CH-R (diamidino stilbene), exhibited a truly remarkable trypanocidal effect on mice infected with our laboratory strain of *T. rhodesiense*. When administered intraperitoneally the maximum dose tolerated by mice is in each case about 1 mgm. per 20 gm. mouse. With the most active compound, 4 : 4′-R-CH : CH-R, such minute doses

as 0·005 and 0·00625 mgm. per 20 gm. mouse suffice to clear the peripheral blood of trypanosomes in more than 50 per cent. of cases; permanent cures are obtained with doses of 0·01 and 0·0125 mgm., and with doses of 0·025 and 0·05 mgm. the great majority of animals are cured. The therapeutic index $\left(\frac{\text{Maximum tolerated dose}}{\text{Minimum curative dose}}\right)$ of 4 : 4′-diamidino stilbene is accordingly about 30. The other two compounds, viz., 4 : 4′-R-O$(CH_2)_5$O-R and 4 : 4′-R-O$(CH_2)_3$O-R, are only slightly less active. This degree of trypanocidal activity surpasses that of any of the aromatic arsenicals.

"Tests on rabbits in an advanced stage of infection with the same trypanosome gave equally striking results. The maximum dose tolerated by rabbits when treated intravenously is about 20 mgm. per kilo. With 4 : 4′-R-CH : CH-R, single doses of 1·25 to 5 mgm. per kilo. cured the majority of animals, and repeated small doses gave even better results, 0·5 mgm. (i.e., 1/40th of the maximum tolerated dose) repeated on each of 5 consecutive days curing all of 8 rabbits. The results obtained with the other two compounds are nearly as good.

"While many of the compounds displayed some action on *T. congolense* infections in mice, cures were obtained only with 4 : 4′-R-CH : CH-R, and then only when the drug was given in maximum doses; all of 7 mice were cured by a single dose of 1·0 mgm., and 2 of 7 by a dose of 0·5 mgm. Repeated fractional doses gave better results, all of 9 mice being cured by 0·25 mgm. given on each of 3 consecutive days.

"None of the compounds had any action on *T. cruzi* infections of mice, nor on infections due to *Spirochaeta recurrentis* or *Spirillum minus*. Certain of them, however, exhibit a remarkable activity against other protozoal infections, notably those due to Leishmania and Babesia, but this will be discussed in subsequent papers.

"Some description is given of the toxic manifestations exhibited by various animals and by man after the administration of relatively large doses of these aromatic diamidines." *W. Y.*

LOURIE (E. M.) & YORKE (Warrington). **Studies in Chemotherapy. XXII.—The Action of Certain Aromatic Diamidines on** *Babesia canis* **Infections of Puppies.**—*Ann. Trop. Med. & Parasit.* 1939. Dec. 30. Vol. 33. Nos. 3 & 4. pp. 305–312. [11 refs.]

Attention is drawn to the fact that very little progress in the therapy of Babesia infections has been made since NUTTALL's discovery in 1909 of the activity of trypan blue. STEPHAN and ESQUIBEL, in 1929, showed that acriflavine also exerted a definite action on certain Babesia infections, but the first real advance in the therapy of this group of diseases was made in 1935, when KIKUTH and others published accounts of very successful results obtained with a Bayer product known as acaprin.

Several years ago, Lourie and Yorke had noticed that certain aliphatic diamidines, particularly n. undecane diamidine, exerted a definite action in *Babesia canis* infections of puppies, but that cures could not be obtained with this compound. This observation encouraged the authors to inquire whether the more powerfully trypanocidal aromatic diamidines had any action on *Babesia canis*. The present paper records the results of these experiments. The following summary is given :—

"1. Most of the aromatic diamidine compounds examined had a definite action on *Babesia canis* infections of puppies in that they caused the blood to become negative for a time.

"2. The most active compounds were diamidino stilbene (R-CH : CH-R), diamidino diphenyl ether (R-O-R), and diamidino diphenoxy

propane ($R\text{-}O(CH_2)_3O\text{-}R$). Permanent cures could be obtained with single doses of these substances or with two smaller doses given on successive days.

"3. *Babesia canis* could readily be made resistant to these aromatic diamidines, and the drug-resistance persisted unchanged after passage of the parasite through a number of puppies." *W. Y.*

DE BORCHGRAVE (Osc.). Trypanociede werking "in vitro" van "Argoflavine" en "Atebrine." [**Trypanocidal Activity of Argoflavine and Atebrin** *in vitro*.]—*Ann. Soc. Belge de Méd. Trop.* 1939. Dec. 31. Vol. 19. No. 4. pp. 489–493. French summary.

The author summarizes his paper as follows :—

"Although Argoflavine and Atebrin show practically no clinical activity in trypanosomiasis, we have established that Argoflavine in the case of an ordinary strain and of an arsenic-resistant strain of *T. gambiense*, and Atebrin in the case of the latter strain, remove *in vitro* almost instantaneously the power of blood rich in trypanosomes to infect guineapigs, provided that the concentration of the drugs reaches 2 per 1,000. The arsenic-resistant strain is twice as sensitive to Argoflavine as the normal strain; the former becomes avirulent after 20 minutes at a concentration of 1 in 30,000, the latter in the same period only at 1 in 15,000." *C. W.*

DE BORCHGRAVE (Osc.). Photodynamie van "Argoflavine" voor "*Trypanosoma gambiense*." [**Photodynamic Action of Argoflavine on** *T. gambiense*.]—*Ann. Soc. Belge de Méd. Trop.* 1939. Dec. 31. Vol. 19. No. 4. pp. 495–500. French summary.

The author summarizes his paper as follows :—

"1. Under the action of the intense beam of an ordinary arc lamp for dark ground illumination, Argoflavine destroys the motility of *T. gambiense* about ten times more quickly than by diffuse daylight.

"2. This photodynamic action was more intense with an arsenic-resistant strain than with a normal strain. (At the same time, the arsenic-resistant strain was more sensitive than the normal strain to non-irradiated Argoflavine, see above. It should be understood that the difference in sensitivity is not necessarily in proportion to the arsenic-resistance, since the normal strain has been isolated in a guineapig only one year and the arsenic-resistant strain 6 years.)

"3. We have not been able to confirm the phenomenon of the rapid disappearance of the blepharoplast under the influence of acridine derivatives, which has been reported by JANCSO and KOLLE *et al.*

"4. The photodynamic effect may be the result not only of the activation of trypanocidal power of the drug but also of the diminution of resistance of the parasite to light." *C. W.*

i. COON (Arthur B.). **Nitritoid Crises following Tryparsamide Therapy.**—*Arch. Dermat. & Syph.* 1939. Oct. Vol. 40. No. 4. pp. 601–602.

ii. ELLIS (Francis A.). **Nitritoid Reactions due to Tryparsamide. Report of a Case.**—*Ibid.* 1939. Nov. Vol. 40. No. 5. pp. 707–708.

i. Coon reports two nitritoid reactions developing in a syphilitic during the course of tryparsamide treatment. The patient contracted syphilis in 1925, for which he had irregular and inadequate treatment. In 1936, he consulted the author, with signs of neurosyphilis, for which

he received vigorous, uninterrupted antisyphilitic treatment with bismuth, iodides, arsphenamine and tryparsamide. By September 1937 he had had 39 injections of tryparsamide, and as lumbar puncture still showed a pathological spinal fluid the patient was treated with malaria. Tryparsamide treatment was resumed in January 1938, at which time the patient had greatly improved.

After the tenth injection of this course the patient felt weak, faint and nauseated, the pulse was accelerated and marked congestion of the conjunctiva, face and neck supervened. He soon recovered, and tryparsamide was withheld for five months. No untoward reaction followed the subsequent course of tryparsamide until the ninth injection (58th of the series, 167 gm.) when there occurred immediate extreme congestion of the conjunctiva, face and neck, acceleration of the pulse and respiration, depression, nausea, desire to defaecate, and itching of the face, neck, trunk and arms. After 30 minutes' rest, the patient recovered sufficiently to return home. The next day he reported that he had had a rigor, weakness, nausea and a desire to defaecate. The rigor, which lasted 90 minutes, was followed by a high temperature of several hours' duration, prostration, and numerous weals on the chest, abdomen and arms. The next morning the condition had returned to normal.

ii. Ellis records a somewhat similar reaction in a neuro-syphilitic who was given malaria treatment in 1933, and between February 1934 and March 1939 had no fewer than 148 injections of tryparsamide of 3 gm. each. Only after the 113th injection did the patient experience mild vasomotor reactions, characterized by flushing of the face and neck. After subsequent treatment the symptoms became more severe, and there was a constricted feeling in the chest, accompanied by a cough and throbbing of the head. The more severe reactions lasted 30 to 45 minutes.

After the last injection of tryparsamide (2 gm.) there was definite flushing of the face; the patient had a sense of impending disaster and a tight feeling in the chest. In ten minutes he began to cough and vomit. Soon there developed severe cramps in the abdomen and these were followed by involuntary movements of the bowel and bladder. In 30 minutes the symptoms began to abate. The blood pressure and pulse varied but slightly during the attack. *W. Y.*

CULBERTSON (James T.) & WOTTON (Robert M.). **Studies on Age Resistance against Trypanosome Infections. VI. Production of Ablastin in Rats of Different Age Groups after Infection with** *Trypanosoma lewisi.—Amer. Jl. Hyg.* 1939. Nov. Vol. 30. No. 3. Sect. C. pp. 101–113. With 2 graphs. [14 refs.]

This paper records the results of a study comparing the production of ablastin [an antibody inhibiting trypanosome reproduction, *vide* this *Bulletin*, 1933, Vol. 30, p. 122, and 1939, Vol. 36, p. 214] in rats of different age groups following infection witn *T. lewisi*. According to TALIAFERRO, this antibody is an important factor in the resistance of the adult rat to infection with *T. lewisi*; it appears in the serum about the fourth or fifth day after infection and gradually increases in amount in the blood until the host is cleared of the infection. It persists in the blood of recovered animals and seems to account for the lifelong immunity to re-infection which recovered rats enjoy.

In the experiments described in the present paper, rats of different age groups have been carefully tested for their capacity to produce ablastin. The following are the conclusions :—

" Rats 25 days of age or more, when infected with *Trypanosoma lewisi*, generally produce the ablastin antibody well and usually survive the infection. Rats below this age, when infected, generally produce the ablastin antibody poorly or not at all and usually succumb to *Tryp. lewisi* infection.

" Although other factors also doubtless play a significant rôle in the acquisition of resistance with age, it is concluded that the greater capacity of the older rat to form the ablastin antibody is a major factor in the greater resistance of older rats to infection with *Trypanosoma lewisi*."

*W. Y.*

KOLODNY (Maxwell H.). **Studies on Age Resistance against Trypanosome Infections. VII. The Influence of Age upon the Immunological Response of Rats to Infection with** *Trypanosoma cruzi*.—*Amer. Jl. Hyg.* 1940. Jan. Vol. 31. No. 1. Sect. C. pp. 1–8. With 1 fig. [11 refs.]

CULBERTSON and WOTTON [see above] have described the immunological response of rats of different ages to an active infection with *T. lewisi*, and have shown that the capacity of rats to produce ablastin antibody increases with age ; it was pointed out that this antibody is seriously deficient in nurslings and that these animals usually succumbed to the infection. Kolodny has investigated the point in *T. cruzi* infections of rats of different ages ; he summarizes his conclusions as follows :—

" The capacity of rats to produce an immune response after infection with *T. cruzi* is influenced by the age of the animal at the time of its infection.

" Young suckling rats up to 20 days of age are unable to respond to this infection at any time before their death with the production of a sufficient quantity of protective antibodies to be demonstrable by the protection-test method.

" Recently weaned rats, 30 days of age at infection, produce antibodies that are first demonstrable about 15 days following infection. In these animals the antibody titer increases progressively and about 35 days after infection attains a maximum which is definitely lower than that reached by older animals.

" Young adult rats 60 days of age and fully mature rats 85 days to 100 days of age produce antibodies that are first demonstrable about 8 days after infection. Thereafter, the antibody titer increases progressively, but somewhat more rapidly in the fully mature rats. The final antibody titer 35 days after infection is, for all practical purposes, the same in animals of both age groups.

" The inability of nursling rats to develop demonstrable quantities of protective circulating antibodies, and the gradual perfection with age of this immunological response substantiates the previously reported observations on the functional immaturity of the antibody-forming mechanisms of very young animals. Development of these protective antibodies appears to be one of the important defense mechanisms of the host inasmuch as recovery, as a rule, follows the appearance of these immune bodies.

" The period of maximum immunological activity occurs concomitantly with the onset of physiological maturity."

*W. Y.*

CULBERTSON (James T.). **The Natural Transmission of Immunity against *Trypanosoma duttoni* from Mother Mice to their Young.**—*Jl. Immunology.* 1940. Jan. Vol. 38. No. 1. pp. 51–66. [14 refs.]

It is now established upon a sound basis that immune mothers do confer resistance to their young against specific infections, and in some cases the survival of the young is contingent upon the transfer of protective substances to them from the mother. This might occur either through the placental circulation or through the milk. Evidence has been accumulated which indicates that different species of animals differ fundamentally as to which of these two possible routes of transmission of protective substances is the principal one.

Previous work by the author and KOLODNY has shown that in the case of *T. lewisi* and *T. cruzi* infections of rats, the transfer of antibody from the mother to the young was attained by the young almost entirely through the ingestion of the mother's milk. [This *Bulletin*, 1939, Vol. 36, p. 751, and 1940, Vol. 37, p. 143.]

The present paper records the results of a similar study carried out in the mouse, with a natural mouse parasite, *T. duttoni*. The author summarizes his results as follows :—

" Mother mice which have recovered from an infection with *Tryp. duttoni* transmit to their young protective substances which render the young resistant to infection with this parasite. The young animals acquire their resistance principally after birth through the ingestion of milk from the immune mother. The young born of a normal mother promptly acquire resistance against *Tryp. duttoni* if permitted to nurse the specifically immune mother.

" The immune substances are secreted by the mother not only in the colostrum, but also in the milk later passed, and nurslings until 15 days old as well as those newly born can absorb the protective substances from the intestine after ingesting the milk of the immune mother. Accordingly, it is possible for a mother who has been infected after the birth of her litter to develop and transmit protective substances to her nurslings in sufficient amount to protect them measurably against a subsequent infection.

" A mother mouse passively immunized by the injection of serum from a mouse which has recovered from *Tryp. duttoni* is also able to transmit protective substances to the young which nurse her.

" The immunity of the young mice is specific, and nurslings injected with *Tryp. cruzi* will become infected even though they nurse a mother immune to *Tryp. duttoni*.

" It is pointed out, in discussion, that the mouse differs as to the principal route of transfer of the protective substances to the young from that generally accepted for hemochorial mammals." *W. Y.*

ACANFORA (Giuseppe). Tentativi di infezione sperimentale dell' embrione di pollo con *Castellanella brucei*. [**Experimental Infection of Fowl Embryo with** *T. brucei*.]—*Arch. Ital. Sci. Med. Colon. e Parassit.* 1939. Oct. Vol. 20. No. 10. pp. 577–591. With 2 charts & 7 figs.

The author shows that it is possible to infect the blood of fowl embryo with *T. brucei* and that multiplication may take place, though only 5 per cent. of the attempts are successful and only if the inoculation is made between the 8th and 14th days of incubation. The trypanosomes multiply rapidly for 3 to 4 days, proportionately to the number

injected, then the number remains stationary for about 48 hours and after that the trypanosomes disappear suddenly and completely. The embryo does not always die and in some cases the parasites undergo a degenerative process before disappearing from the circulation.

*C. W.*

BIOCCA (E.). Essais de vaccination contre le *T. brucei* chez les cobayes moyennant une bouillie d'embryon de poulet infecté, conservée en glacière. [**Attempts to vaccinate Guinea Pigs against** *T. brucei* **by Means of Emulsions of Infected Chick Embryo preserved on Ice.**]—*Boll. Sezione Ital., Soc. Internaz. di Microbiologia.* Milan. 1939. May–June. Vol. 11. No. 5–6. pp. 136–137.

In the experiments recorded in this paper, the author has inquired whether a suspension of chick embryo, 15 to 16 days after infection with *T. brucei*, preserved for various periods on ice and then inoculated intraperitoneally into guineapigs, would increase the resistance of the guineapigs to subsequent infection with *T. brucei*.

It was found that 0·1 cc. of suspension, kept for 3 to 5 days on ice, increased the resistance of the guineapigs in so far as it prolonged the course of the disease when they were subsequently inoculated with *T. brucei*. In 9 control observations, the animals died in from 6 to 13 days, whereas the 7 vaccinated animals lived for 33 to 59 days.

*W. Y.*

VAN DEN BRANDEN (F.). Le sang des lapins infectés de trypanosoma "Brucei" renferme-t-il des réagines de Wassermann et possède-t-il des propriétés floculentes? [**Does the Blood of Rabbits infected with** *T. brucei* **give a Positive Wassermann Reaction and does it exhibit Flocculating Properties?**]—*Ann. Soc. Belge de Méd. Trop.* 1939. Dec. 31. Vol. 19. No. 4. pp. 595–600.

Reference is made to the fact that LANDSTEINER and VAN DER SCHEER (1927) obtained complement fixation and a positive flocculation (Sachs-Georgi) reaction with the blood of rabbits experimentally infected with *T. equiperdum* and also with that of rabbits inoculated intravenously with dead trypanosomes.

As van den Branden had at his disposal rabbits infected many months with *T. brucei*, he decided to examine the complement fixation reaction; he used as antigen an alcoholic extract of *T. brucei* and also an alcoholic extract of calf's heart.

It was found that with the normal rabbit the complement fixation reaction was negative, whichever antigen was employed, whereas with the infected rabbits the reaction was positive with the trypanosome antigen and negative with the heart antigen. The flocculation test (Kahn) was positive in 38 per cent. of normal animals and in 41·6 per cent. of infected animals.

*W. Y.*

DUBOIS (A.) & KOHN (I.). A propos du mode d'action de l'arsénobenzène sur les trypanosomes. [**The Mode of Action of Arsenobenzol on Trypanosomes.**]—*Ann. Soc. Belge de Méd. Trop.* 1939. Dec. 31. Vol. 19. No. 4. pp. 501–512. [11 refs.]

In this article the authors have refrained from a discussion of the vast subject of the mode of action of therapeutic substances, but

limit themselves to a consideration of the mechanism of action of arsenobenzol on *T. brucei*. It is generally admitted that the mode of action of this substance is direct, since YORKE and MURGATROYD [this *Bulletin*, 1931, Vol. 28, p. 350] demonstrated that it killed trypanosomes *in vitro* in great dilutions.

Dubois and Kohn have confirmed this conclusion by a simple technique which consisted briefly in injecting a heavily infected mouse with a large dose of "914" intravenously, and then after various intervals (5 to 20 minutes) inoculating healthy mice with the blood of the infected and treated mouse. It was found, for example, that only 5 minutes after the treatment (4·5 or 3 mgm. of arsenobenzol) of a heavily infected mouse, its trypanosomes were no longer infective when injected into normal mice. The trypanosomes had consequently fixed a fatal dose of the drug within a very short period, so that any question of the intervention of the defence forces of the organism can be excluded.

The problem whether 914 acts as such or after transformation (into arsenoxide) in the body of the host is, however, still unsettled. The action of 914 is moderately rapid, whilst that of arsenoxide or of the products of oxidation of arsenobenzol is much more rapid. This fact, which the authors have confirmed, seems rather to favour a transformation.

The authors were able to discover little difference between the rapidity of action of 914 when administered intravenously and when given subcutaneously. There is, however, no doubt that the compound is much more toxic when given by the latter route, and this suggests that it undergoes chemical change when given subcutaneously; nevertheless the rapidity of sterilization and the efficacy are not materially increased.

The action of 914 was found to be retarded by methylene blue. This can be interpreted as due to an inhibition of its oxidization, but it must be confessed that the existence of toxic phenomena makes the interpretation difficult, and that a redox system, such as ascorbic acid, is apparently much less active.

The non-infectivity of trypanosomes some minutes after treatment of the infected animal does not seem to favour the necessity of oxidation of 914; but of course the compound may be oxidized inside the body of the parasite. *W. Y.*

DUBOIS (A.) & LOSNER (S.). L'élimination de l'arsénobenzène chez les animaux normaux et à système réticulo-endothélial bloqué. [**The Elimination of Arsenobenzol in the Normal Animal and in Animals in which the Reticulo-Endothelium is Blocked.**]—*Ann. Soc. Belge de Méd. Trop.* 1939. Dec. 31. Vol. 19. No. 4. pp. 513–525. With 1 chart.

Details are given of 11 experiments in which estimations of arsenic in the blood were made, in rabbits and rats, at intervals after the administration of 914. In certain of these experimental animals the reticulo-endothelium was blocked by splenectomy combined with intravenous injection of Chinese ink or electro-colloidal copper. The technique used for estimation of the arsenic content of the blood was that of Beck and Merres; it is described in some detail.

The results obtained showed that arsenic could be found up to 24 hours in traces sufficient to explain trypanocidal action. The

results are compared with those obtained by MURGATROYD, RUSSELL and YORKE, who examined the trypanocidal activity of the blood of normal rabbits after the administration of novarsenobillon and other arsenicals [this *Bulletin*, 1935, Vol. 32, p. 26]. The observations agree closely.

Blockade of the reticulo-endothelium system did not appear to produce any constant change in the result. *W. Y.*

RICHET (Charles) & ANTOINE (Georges). Immunisation chimiobiologique des rats blancs contre le "*Trypanosoma equiperdum*." [**Chemobiological Immunization of White Rats against** *T. equiperdum*.]—*Bull. Acad. Méd.* 1939. Nov. 28 & Dec. 5. 103rd Year. 3rd Ser. Vol. 122. No. 33. pp. 471–477.

Rats inoculated subcutaneously with a virulent strain of *T. equiperdum* were treated when trypanosomes appeared in the blood with a curative dose of sulpharsenol, and then after various intervals were re-injected subcutaneously with the same trypanosome. It was found that between 36 and 60 days, 17 of 30 animals were completely immune, and 12 partially immune; between 61 and 100 days, 21 of 22 animals were completely immune and 1 partially immune; and between 101 and 240 days, 9 of 14 were completely immune and 5 exhibited no immunity. *W. Y.*

KRANEVELD (F. C.) & UMBOH (Th. E. W.). Experimenten over het gefractionneerd toedienen van naganol bij de behandeling van surra. [**Fractional Administration of Naganol in the Treatment of Surra.**]—*Nederl. Indische Bladen v. Diergeneesk.* 1939. Dec. Vol. 51. No. 6. pp. 371–383. With 2 figs. English summary.

"Under conditions which were kept as far as possible uniform (experimental animals from the same breeder, of practically the same age and weight, infected with the same number of trypanosomes all of one strain obtained from a single ancestor and showing practically identical courses of infection) the therapeutic effect of definite doses of naganol in guineapigs suffering from surra showed differences. There is, therefore, an 'individual' difference, with which account must be taken in designing experiments concerning naganol-resistance, etc.

"It can be shown by experiments with guineapigs, that the therapeutic effect of a certain dose of naganol is less if the dose is given in fractional parts with a day's interval between injections. Again, the larger the number of times the dose is subdivided the less the number of cures." [See also this *Bulletin*, 1939, Vol. 36, p. 744.]

"It can be shown in horses that a part of the naganol, or a trypanocidal product thereof, is excreted in the urine shortly after injection. In guineapigs, which were injected, at a time when there were many surra trypanosomes circulating in their peripheral blood, with 5 cc. of such a urine specimen passed between 5 and 37½ hours after an intravenous injection of naganol, the parasites disappeared rapidly from the blood, a state of affairs which persisted for a number of days (even as long as 33).

"Normal urine specimens of two out of the three horses used in making the experiments proved also to have an effect on the surra trypanosomes *in vivo*, but to a much less degree. The cause of this could not be attributed to the pH of the urines nor to their urea contents."

MAZZA (Salvador). La enfermedad de Chagas en la República Argentina. [**Chagas's Disease in the Argentine Republic.**]—Reprinted from *Las Actas y Trabajos del VI Congreso Nacional de Medicina, Cordoba.* 1939. Vol. 3. 14 pp. With 1 map.

In this article Professor Mazza gives a *résumé* of the prevalence of Chagas's disease in the Argentine and the hosts of the parasite. In the sixteen provinces there had been 370 reported up to the end of June 1938. Nearly one-third had occurred in Mendoza (106), Chaco coming next (67) and then Santa Fe (64). In the last-named cases had been seen in every month, whereas none had been reported from Mendoza in the four months June–September inclusive. Of the total, 345 had been diagnosed directly by examination of the blood in thick drops, 9 by inoculation, 14 by the xeno-diagnostic method, and 2 by examination of an excised gland. The following animals had been found naturally infected: *Canis familiaris* and *Felis domesticus* among the domestic animals; of Edentates *Chaetophractus vellerosus vellerosus* in Jujuy; *C. v. pannosus* in San Juan; *C. villosus* in Formosa; *Zaedyus pichyi caurinus* in Mendoza; *Tolypeutes matacos* in Salta and Formosa; *Dasypus novemcinctus* in Chaco and Santa Fe; of Marsupials, *Didelphis paraguayensis* in Santa Fe and Salta, and *Lutreolina crassicaudata paranalis* in Santa Fe; *Pseudalopex culpeus culpeus* in Mendoza; and of the Mustelidae, *Grisonella ratellina* in Mendoza and *G. huronax* in Santa Fe. Insect vectors are notably *Triatoma infestans*, *T. platensis*, *T. rosenbuschi* and *Eutriatoma sordida* and *E. oswaldoi*.

*H. H. S.*

MAZZA (Salvador). Enfermedad de Chagas en San Juan. Consideraciones generales. [**Chagas's Disease in San Juan.**]—*Prensa Méd. Argentina.* 1940. Feb. 21. Vol. 27. No. 8. pp. 401–410.

ROUBAUD (E.) & ROMAÑA (J.). Infection de l'embryon de poule par *Schizotrypanum cruzi.* (Note préliminaire.) [**Infection of the Fowl Embryo with** *T. cruzi.*]—*Bull. Soc. Path. Exot.* 1939. Nov. 8. Vol. 32. No. 9. pp. 874–875.

It is now known that although the fowl is but slightly susceptible to the trypanosomes pathogenic to man and stock, its embryo is, on the contrary, easily and regularly infected [this *Bulletin*, 1940, Vol. 37, p. 12]. It is also known that the fowl cannot be infected with *T. cruzi*, and the authors have now examined whether the embryo is susceptible.

Three experiments are recorded, and controls were performed with *T. dimorphon* and *T. gambiense.* In the controls the embryos were readily infected and a week later numerous trypanosomes were formed in a state of multiplication. In only a single instance, however, was *T. cruzi* found in an embryo 7 days after inoculation. The authors conclude from this that if they have not succeeded in demonstrating that *T. cruzi* can multiply in the fowl embryo as can other trypanosomes, they have shown that *T. cruzi* can survive in the fowl embryo for a week.

*W. Y.*

GASIC (Gabriel). Indice de infestación por *Trypanosoma cruzi* de los Triatomides de la provincia de Coquimbo. [**Degree of Infestation of Triatoma by *T. cruzi* in the Province of Coquimbo.**]—*Rev. Chilena de Hig. y Med. Preventiva.* 1939. Jan.–Mar. Vol. 2. No. 1–3. pp. 17–20.

Specimens of *Triatoma infestans* in three districts of the Province were examined. In Illapel of 288 captured 158 (54 per cent.) were infected—124 of 179 adults and 34 of 109 larvae or nymphs. In Ovalle 102 of 167 adults (60 per cent.) and 72 of 184 larvae and nymphs (39 per cent.) or, together, 174 out of 351 (49 per cent.). In Elqui department 185 were positive out of 364 (50 per cent.), 113 out of 188 adults (60) and 72 out of 176 larvae and nymphs (40 per cent.). It was at Paihuana in this department that the first acute case of Chagas's disease in Chile was reported. In the Province, therefore, from examination of 534 adults and 469 larval stages, or 1,003 in all, 517, or 51 per cent., were found infected. *H. H. S.*

HOFFMANN (W. H.). Experiencias biologicas sobre los triatomas de Cuba. [**On Cuban Triatomata.**]—*Rev. Med. Trop. y Parasit.* Habana. 1939. Sept.–Oct. Vol. 5. No. 5. pp. 267–272.

The author describes the *Triatoma flavida*, a Reduviid found, he states, only in Cuba and even there restricted to certain districts; Oriente, Camagüey and the mountainous parts of Pinar del Rio. It is the largest of the Cuban Reduviids [the author gives its length as 24–39 cm., truly a formidable "whale of a bug" (he probably means mm.)], is a blood-sucker and experimentally acts as a vector of *T. cruzi*. Examination of many specimens caught has not yet revealed any naturally infected with trypanosomes, but should a patient be introduced into the island, the risk of the disease obtaining a hold is great seeing that the potential vector already exists.

The author calls for further study to determine more accurately the distribution of *Triatoma flavida* and for vigilance against admission of patients harbouring *T. cruzi*. *H. H. S.*

MAZZA (Salvador), BASSO (Germinal), BASSO (Redento) & JÖRG (Miguel Eduardo). Investigaciones sobre la enfermedad de Chagas. I. Primer caso mortal de forma crónica cardíaca de enfermedad de Chagas, comprobado en Mendoza. [**Chagas's Disease. I. First Fatal Case of the Chronic Cardiac Form seen in Mendoza.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 42.* 1939. pp. 1–73. With 83 figs. & 1 coloured plate. [10 refs.]

This is a very detailed account of the pathological anatomy and histology of the lesions found in a woman of 21 years with microcephaly, enlarged thyroid, absence of the left hand and other congenital deformities who suffered from certain heart symptoms, asthma, etc., and died 18 months after the beginning of her cardiac symptoms. The article is purely of pathological interest and the descriptions of the changes found cannot be summarized. It is illustrated by three photographs, three teleradiographs, more than a score of electrocardiograms, a coloured plate and 70 photomicrographs. *H. H. S.*

MAZZA (Salvador) & JÖRG (Miguel Eduardo). Investigaciones sobre la enfermedad de Chagas. II. Diferencias entre anatomía patológica de carditis reumática y carditis de enfermedad de Chagas. [**Chagas's Disease. II. The Cardiac Lesions of Chagas's Disease compared with those due to Rheumatism.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 42.* 1939. pp. 74–97. With 12 figs. [24 refs.]

This, like the last, deals solely, as the title implies, with morbid histology; the differences, which in some respects are questions of degree, are described in detail in the text and the fundamental qualitative differences are presented in a table under the headings of (1) Exudative and "katabiotic" changes; (2) Bioplastic phenomena, re-absorption, proliferation and cellular differences; (3) Evolution leading in the rheumatic form to nodular, sclerotic scars and, in some cases, to larger sclerotic areas, multifocal and perivascular; in Chagas's disease to diffuse sclerosis with slender collagen fibrils with necrobiotic foci and irregularly distributed giant cells in zones of infiltration, with myeloid and eosinophil cells. *H. H. S.*

ALBERTO AGUIRRE (Juan) & GIMENEZ (Clodomiro). Consideraciones de semiología radiológica sobre 168 roentgencardiometrías en la enfermedad de Chagas. [**Radiology of the Heart in Chagas's Disease.**]—Reprinted from *Las Actas y Trabajos del VI Congreso Nacional de Medicina Cordoba.* 1939. Vol. 3. 7 pp.

Though this article analyses 168 radiograms only 61 patients were examined, ranging in age from 3 to 64 years, but 54 of them were below 14 years. All but 7 showed recognizable changes by X-ray, enlargement of both ventricles, more particularly the left; this enlargement progressed with the disease and might reach double the normal size, but diminished again under treatment, particularly with rest and digitalis. In some cases there were periodic enlargements of more sudden onset, as if the heart were undergoing acute dilatation ascribable to myopathy. *H. H. S.*

MAZZA (Salvador). Métodos de investigación de la epidemiología de la enfermedad de Chagas. La viscerotomía cardio-hepática. [**The Viscerotome as an Aid in studying the Prevalence of Chagas's Disease.**]—*Prensa Méd. Argentina.* 1939. Dec. 20. Vol. 26. No. 51. pp. 2461–2470. [22 refs.]

After discussing the value of xenodiagnostic methods and of the Machado-Guerreiro reaction in the diagnosis of Chagas's disease, the author describes certain changes in the liver which he regards as pathognomonic of this disease. These are nodular formations, mostly in the middle of the lobules, made up of accumulated lymphocytes in a thick network of reticular histiocytes, which dissociate the tissue and appear on section as circular foci. This *nodular hepatitis* with proliferation of histiocytes in an indurated, passively congested liver is, he states, of diagnostic importance. In the same way as the viscerotome has proved its value in the epidemiology of yellow fever, so it is as regards Chagas's disease by enabling sections to be made of the liver tissue to demonstrate characteristic pathological changes. At the same time as the liver tissue is taken, the opportunity may be seized

to take a portion of the cardiac muscle and to show the presence of the parasite there also. Dr. PONS reported to the author in November 1939 that in the first five " cardiac viscerotomies " performed, three (all children) had revealed the characteristic findings of Chagas's disease. *H. H. S.*

ROMAÑA (C.). Le parasitisme des cellules epithéliales de la conjonctive du singe par *Schizotrypanum cruzi*. [**Parasitism of the Conjunctival Epithelium of a Monkey by** *T. cruzi*.]—*Bull. Soc. Path. Exot.* 1939. Oct. 11. Vol. 32. No. 8. pp. 810–813. With 1 fig.

A monkey infected with *T. cruzi* by the deposition of the infected faeces of *Rhodnius prolixus* on the conjunctiva was killed 12 days after parasites had appeared in the peripheral blood. Histological examination of the organs revealed the presence of leishmanoid forms of the parasite in the heart, liver, spleen, suprarenals, kidneys, muscles, meninges and salivary glands ; and cellular infiltration consisting of lymphocytes, plasmocytes and histiocytes.

The eye which served as the portal of entry of the infection was also carefully examined. There was hyperplasia of the oculo-palpebral epithelium ; the cylindrical epithelial cells were tumified, and some of them were parasitized with leishmanoid forms of *T. cruzi*. In some places the superficial layers of epithelium had disappeared. The conjunctiva was infiltrated with lymphocytes, plasmocytes and histiocytes, and in places presented a nodular appearance. The capillaries were dilated and congested, and several lymphatics were likewise dilated. Many of the histiocytes were loaded with parasites. The peri-ocular conjunctiva exhibited similar areas of infiltration, but the various tissues constituting the globe itself showed no pathological changes. *W. Y.*

LEITE (A. Lobo). Doença de Chagas e bocio endemico. [**Chagas's Disease and Endemic Goitre.**]—*Brasil-Medico.* 1939. Nov. 11. Vol. 53. No. 46. pp. 1031–1033.

[After the investigations of KRAUS, ROSENBUSCH & MAGGIO (see this *Bulletin*, 1916, Vol. 7, p. 115, and 1926, Vol. 23, p. 912) and the able summing up of the question by Cecilio ROMAÑA (this *Bulletin*, 1935, Vol. 32, p. 720) and finally the verdict of Dr. Evandro Chagas, the son of Carlos Chagas, as the outcome of an intensive study of the disease in 1935 that " the disease occurs in goitrous districts . . . . but the older idea that there was a goitrous form of the disease is no longer maintained. Up to the present time there has been no experimental work confirmatory of Carlos Chagas's theory that the goitre occurring in these regions is due to infection by *Trypanosoma cruzi* " (this *Bulletin*, 1936, Vol. 33, p. 675) it seems surprising that the matter should on clinical and epidemiological grounds be thought worthy of further consideration].

The author records the results of 71 cases of goitre in which the serum was subjected to the Machado-Guerreiro complement fixation reaction. Thirty-seven were tested by Dr. Lacorte ; 35 were negative, one positive and one doubtful ; of seven tested by Dr. Villela six were negative and one positive ; of 27 tested by the author 24 were negative, three positive. Thus of the whole, 65 were negative, 5 positive, one doubtful. Further enquiry showed that all those whose sera were

positive had previously lived in infested districts, one in Joatuba, west of Minas, and four in Itaverava. The author concludes that "the occurrence of goitre in patients suffering from American trypanosomiasis cannot be considered as an essential part of the picture of the disease." *H. H. S.*

DIAS (Emmanuel). O signal de Romaña e sua influencia na evolução dos conhecimentos sobre a molestia de Chagas. [**Romaña's Sign and its Influence on the Development of Knowledge of Chagas's Disease.**]—*Brasil-Medico.* 1939. Oct. 14. Vol. 53. No. 42. pp. 965–970. [34 refs.]

GASIĆ (Gabriel). Enfermedad de Chagas. [**Chagas's Disease.**]—*Rev. Chilena de Hig. y Med. Preventiva.* 1939. Apr.–June. Vol. 2. No. 4–6. pp. 117–168. With 23 figs. [35 refs.]

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## PLAGUE.

### *Précis* of Abstracts in this Section.

RAO (p. 418) shows that in Nalgonda and Hyderabad the *R. rattus* population is the same, but in Nalgonda the flea is *X. astia* and in Hyderabad *X. cheopis*. The climate of Nalgonda is hot and dry and probably the effect of this on the susceptible *X. astia* is responsible for the fact that plague does not exist, though it is common in Hyderabad.

VAN HOOF (p. 419) reports on a new focus of plague in the Belgian Congo in which, though *X. cheopis* was absent, the bacilli were isolated from a number of other fleas and from rodents and man. VAN RIEL and MOL (p. 419) found *Mastomys ugandae* and *R. r. alexandrinus* to be the carriers, and *X. brasiliensis* to be the vector in a focus in the Congo which takes its origin from East Africa.

WATS *et al.* (p. 420) working on the production of sera and suspensions of *P. pestis* for immunological work, have observed differences in behaviour according to whether the growth of the organism was effected at 27°C. or 37°C. SOKHEY (p. 420) gives the results of a study of *P. pestis* in which he discusses cultivation, the counting of viable organisms, the preparation of a constant infective test dose, the measurement of virulence and the maintenance of virulence. Consideration of these points is essential in any attempt to assay the value of vaccines. RUSSO (p. 422) records investigations on the fermentation reactions of *P. pestis*, and GIRARD (p. 422) discusses nitrite production.

SAVINO *et al.* (p. 422) having isolated a new species of Pasteurella from rats in S. America, point out that it is not safe to diagnose plague in rats without complete cultural tests for *P. pestis*.

SUÁREZ (p. 423) has found *P. pestis* in throat smears from a number of contacts of cases of pneumonic plague in Ecuador. These latent cases are probably responsible for epidemic outbreaks and special search and treatment should be instituted to deal with them. On the other hand SÁENZ (p. 423) writes of the importance of the guineapig type of rodent in connexion with these epidemic outbreaks. DE LA BARRERA (p. 423) discusses sylvatic plague in the Argentine and names the rodents concerned; their fleas have been shown capable of transmitting the disease. In the *Boletin Sanitario* (p. 424) it is pointed out that in the Argentine a rodent of the genus Sylvilagus is extensively

affected with plague which it may transmit directly to man, or much more commonly to the black rat. MEYER (p. 424) points out the superiority of the investigation of pools of fleas, lice and ticks over the examination of rodents in the investigation of sylvatic plague.

MACCHIAVELLO (p. 424) considers that the rat is the principal reservoir of plague in Chile in the interepidemic periods, but that the recurrence in cycles of acute epidemics is due to reintroduction of infected fleas in bales of jute from India.

He (p. 425) discusses the pathology of rat plague.

ROSIER (p. 425) gives figures showing the decline of plague in Java during 1938. The death rate remains very high. Vaccination with Otten's living vaccine was energetically carried out and in the housing campaign 54,548 new houses were built. SOERONO (p. 426) describes the voluntary house improvement campaign in the district of Madja in Java. No compulsion other than official propaganda is employed but by March 1939, 99·62 per cent. of the houses had been improved by the owners. The district is exceptional in its wealth, but the author points out that the total disappearance of plague may be an inducement to other districts to follow this example.

SAVINO and ANCHEZAR (p. 426) discuss vaccination with the E.V. and the Tjiwidej strains ; the former, which gives rise to granulations in the spleen of animals inoculated, is superior to the latter in immunizing power.

SOKHEY *et al.* (p. 427) state that fumigation with HCN has always been the most effective method of dealing with rats and fleas, but is dangerous. They comment favourably on " calcid briquettes " as a satisfactory means of applying the gas.

YOKOYAMA (p. 427) discusses the infectivity of various Salmonella for rodents.

DANZEL (p. 427) states that red Scilla has almost a selective action against the rat. *C. W.*

RAO (S. Raghavender). **Studies in the Epidemiology of Plague in H. E. H. the Nizam's Dominions : Comparison of Certain Factors in a Plague-Infected Place with that of Neighbouring Plague-free Area.**—*Indian Med. Gaz.* 1940. Feb. Vol. 75. No. 2. pp. 80–86. With 1 map & 1 fig.

The immunity from plague of various parts of India, and especially its entire East Coast, Eastern Bengal and Assam, has been the subject of much discussion. It occurred to the author that he could get, within the limits of the Nizam's Dominions, two adjacent areas one plague-infected and the other plague-free, which might afford an opportunity to determine the cause of a marked immunity from plague. The two areas were Hyderabad City and Nalgonda town, the former liable to attack every year and the latter free except for imported cases. The rat population, *R. rattus*, was practically the same in both cases but the fleas of Hyderabad were *X. cheopis* and those of Nalgonda were *X. astia*. Both these fleas are capable experimentally of transmitting plague, but *X. astia* is a notoriously inefficient vector, and this inefficiency may be ascribed to its great susceptibility to adverse climatic conditions. There was some indication that the rats of Hyderabad were rather more resistant to plague infection than the Nalgonda rats, but the difference was not of the order which distinguishes the Bombay rat from the Madras rat. Free communication

exists between Nalgonda and the neighbouring infected places, but Nalgonda has a hot dry climate. These factors of high temperature and low humidity acting on so susceptible a flea as *X. astia*, probably explain why Nalgonda has escaped the annual epidemics of Hyderabad.

*W. F. Harvey.*

CONGO BELGE : RAPPORT SUR L'HYGIÈNE PUBLIQUE AU CONGO BELGE PENDANT L'ANNEE 1938 [VAN HOOF (L.).]—[**Plague** pp. 17–19.]

A total of 19 cases of plague with 17 deaths was discovered in the region of Butembo to the west of Lake Edward. Sulphanilamide therapy gave two cures in three cases tried. An examination showed that the human flea is Ctenocephalus, and although this flea is regarded as a bad vector, two strains of the plague bacillus were isolated from it. Moreover other strains were obtained from fleas of this species caught in the dust of native huts. Altogether 31 strains of plague were isolated from fleas of various species (*X. brasiliensis, Ctenocephalus canis*, Sarcopsylla, Ctenophthalmus, *X. cheopis*), 25 from rodents (Mastomys, Leggada, Agricanthis, Lemiscomys, Lophuromys and an unknown species) and 18 from man. Most of the prophylactic vaccination has been carried out with dead vaccine, as the use of living vaccine (E.V.) is still regarded as being on its trial. It is suggested that the limited extent of plague in this new focus may be due to the absence of *X. cheopis*.

*W. F. H.*

VAN RIEL (J.) & MOL (G.). La peste dans le nord du Kivu. [**Plague in the North of Kivu.**]—*Ann. Soc. Belge de Méd. Trop.* 1939. Sept. 30. Vol. 19. No. 3. pp. 453–472. With 3 maps. [26 refs.]

Lake Kivu is in Belgian Congo and on the borders of British territory. To the west is Lake Victoria and to the north west, Uganda. " The focus of plague discovered in 1897 by KOCH and ZUPITZA around Lake Victoria may represent, perhaps, the last trace of the disease from which the pandemics of ancient Egypt took their origin." This is to describe the plague of this region as a primary old standing focus of antiquity and this view is further elaborated by the authors for modern times when they say : " Periodically in Uganda and the neighbouring territories of Kenya and Tanganyika this focus shows renewed activity and becomes the place of origin of a devastating epidemic." The present work contains a general discussion of plague epidemiology with topographical detail and may be summarized in its main points : (1) A new focus of human and rat plague has been discovered in Belgian Congo in the territories of Lubero and Beni ; (2) Twenty strains of the plague bacillus were isolated by the collective method of inoculation of bone marrow of rats into guineapigs. *Mastomys ugandae* and *Rattus rattus alexandrinus* are carriers of plague and *Xenopsylla brasiliensis* is a vector. (3) This focus of plague belongs to the endemic group of East Africa probably by way of the Ituri-Kivu route.

*W. F. H.*

DE OLIVEIRA (Waldomiro). A epidemiologia e profilaxia da peste no estado de São Paulo. [**Plague Epidemiology and Prophylaxis in São Paulo.**]—*Bol. Oficina Sanitaria Panamericana.* 1939. Dec. Vol. 18. No. 12. pp. 1138–1150. With 1 fig. & 2 charts.

This article concerns itself mainly with the activity of the Department of Health, which was represented at the Brazilian Conference

on the Epidemiology of Plague in 1938. It discusses sylvatic plague, laboratory measures, urban and rural prophylaxis and recommends a unified organization, legally established and similar to that in Peru.

*W. F. H.*

WATS (R. C.), WAGLE (P. M.) & PUDUVAL (T. K.). **A Serological Study of Some Strains of** *Pasteurella pestis.*—*Indian Jl. Med. Res.* 1939. Oct. Vol. 27. No. 2. pp. 373–387. [12 refs.]

Most of the attempts hitherto made to show the existence of serologically different strains of *P. pestis* have failed. Nor has the present attempt been any more successful, except in the case of a strain from China. Some of the difficulties, however, of obtaining sera and suspensions for carrying out the technique have been overcome and certain differences in reaction of the organisms revealed according as cultures were incubated at 28°C. or 37°C. Sera were obtained "by inoculating rabbits first subcutaneously and later intravenously with graduated doses of heat-killed (55°C. for 30 minutes) cultures of *P. pestis* grown at room temperature (27°C. to 29°C.) on "acid digest agar" and suspended in normal saline. The preparation of an agglutinable suspension of the bacilli, which when grown at room temperature are salt and serum sensitive, is complicated. A procedure was adopted for bacilli grown at 27°C. and 37°C. respectively, which is designed, by shaking, sedimenting and centrifuging, to obtain a homogeneous fine suspension. Although serological differences in strains could not be detected, a distinct difference was manifest in the type of agglutination obtained when the bacillus was grown at room temperature or 37°C. In the former case agglutination was slow, flakes were small and sediment compact, in the latter rapid, large and voluminous. "The incubator (37°C.) growth is capable of absorbing all agglutinins from the sera obtained by immunizing animals with incubator or room-temperature growths, whereas the room-temperature growth is only capable of removing the antibodies from a serum produced by immunizing animals with room-temperature growth . . . . The incubator (37°C.) growth, when heated at 100°C. for one hour, behaves more or less like a room-temperature growth."

*W. F. H.*

SOKHEY (S. S.). **Experimental Studies in Plague. Part I. Introduction.**—*Indian Jl. Med. Res.* 1939. Oct. Vol. 27. No. 2. pp. 313–319. [27 refs.] **Part II. The Solid Medium of Choice, and the Optimal Temperature of Incubation, for the Growth of the Plague Bacillus.**—*Ibid.* pp. 321–329. With 4 plates. [18 refs.] **Part III. A Method for determining the Number of Viable Plague Organisms in Broth Cultures.**—*Ibid.* pp. 331–340. **Part IV. Experimental Animal of Choice for Plague Work.**—*Ibid.* pp. 341–354. With 4 figs. on 2 plates. **Part V. A Method for measuring the Virulence of Plague Cultures.**—*Ibid.* pp. 355–361. **Part VI. A Method for maintaining the Virulence of** *Pasteurella pestis.*—*Ibid.* pp. 363–371. [22 refs.]

I. In this introduction to a series of articles on plague a critical survey is made of the procedure employed in preparation of vaccine from earliest times to the present day. Criticism is directed not only

to technique but also to the absence of satisfactory statistical assessment of results. "It seems the main difficulty of previous workers was due to the lack of a constant test infective dose, constant both as regards virulence and number of organisms."

Many points that are essential in regard to the vaccine have not been determined or the determination has been faulty. The present studies relate to some of these points.

II. Although the plague bacillus will grow on ordinary nutrient agar, this is not the optimum nor even a suitable medium, as may be shown by attempting to obtain growth from a high dilution of a 48-hour broth culture. With a 1–1,000 dilution no growth is obtainable by planting on ordinary agar and incubating for 48 hours at 27°C., whereas blood-agar medium showed discrete colonies. This fact was turned to good account not only to obtain a count of bacteria per cc. but also for detecting contamination in a brew. Optimum temperatures for growth were determined by plating out on nutrient agar progressive tenth dilutions of a 48-hour broth culture and incubating at 27°C. and 37°C., respectively. With a 27°C. incubation "about 5,000 organisms per sq. cm. . . . must be planted to get any growth at all, but when the plates are incubated at 37·5°C. seeding of 500 organisms . . . is enough to give growth." In the author's summary of the position it is said that: "the addition of defibrinated blood, serum, copper sulphate and sodium sulphite promotes the growth of sparsely seeded *P. pestis* on agar surfaces" and that in the case of a solid medium "the medium of choice is blood agar and the optimal temperature of incubation 37°C., a temperature very unfavourable for the growth of this organism in a liquid medium."

III. The method of counting viable organisms by the number of colonies they produce has been developed and consists in making progressive tenth dilutions of the bacterial suspension, planting 0·05 cc. of a suitable dilution on 40 sq. cm. of blood agar and incubating at 37·5°C. That dilution is preferred for enumeration which gives 10 to 40 discrete colonies. Counts thus made agree closely with results obtained by direct microscopic count or "the biological response of a highly susceptible animal to infection." Other standard conditions are imposed such as the use of equal quantities of the same nutrient broth, the same amount of inoculum, test tube of the same internal diameter, a strictly vertical position in the incubator and a strictly undisturbed state in the incubator.

IV. With the methods of counting the content in bacteria of 48-hour broth cultures described, it has become possible to devise a constant infective test dose. The less constant dose provided by a splenic suspension dose has therefore been superseded. White mice of an inbred strain provide specific, constant and highly susceptible test animals. "About 10 organisms per animal produce a 100 per cent. mortality in the white mouse, whereas 800 to 85,000 organisms were needed in the case of the wild house rat, 40 to 8,500 organisms for the white rat and 6 to over 15 million organisms in the case of the guineapig. As the breeding of white mice under tropical climatic conditions is not altogether simple, an appendix is supplied on the "Breeding and Care of the White Mouse."

V. Measurement of virulence means the determination of the smallest number of organisms which when given subcutaneously, in doses of 0·2 cc. of a dilution of a 48-hour broth culture incubated at 25° to 27°C., to a batch of inbred white mice will kill approximately

100 per cent. of them within 3 to 11 days. " The relative virulence of different strains could be further particularized by the average number of days elapsing between infection and death."

VI. The method of maintaining the virulence of the plague bacillus " consists in planting the strains to be preserved on 5 per cent. rabbit-blood agar slopes in test tubes, incubating them at room temperature (26°C. to 32°C.) for four days and at the end of this period sealing the tubes in the flame and storing them at 4°±2°C." *W. F. H.*

RUSSO (Egydio). Nota adicional á " Contribuição ao estudo fermentativo das bactérias do gênero Pasteurela." [**Fermentation Reactions of** *P. pestis.*]—*Hospital.* Rio de Janeiro. 1940. Jan. Vol. 17. No. 1. pp. 47–51. English summary.

" The paper deals with fermentative tests on carbohydrates carried out with 12 different strains of plague bacillus freshly recovered from natural infection of rats in Rio. Previous distinction from other bacteria belonging to the Pasteurella group of bacteria was accurately established on the basis of experimental tests in animals as well as on serologic tests (agglutination). The writer's principal aim was to compare laboratory stock cultures of *Pasteurella pestis* and freshly recovered ones as to their fermentative behaviour such as already determined in a previous paper (*O Hospital* 16 (1) : 57–66. 1939). As a result it was seen that some differences of both groups of cultures occurred mainly in (1) lactose, (2) rhamnose and (3) sucrose. While stock cultures proved able to ferment lactose very slowly, the recent ones did not so. Inversely most of the latter attacked rhamnose, which remained unchanged in the presence of the former. Finally, a very carefully studied strain of *P. pestis* has been able to form acid from sucrose media on the 15th incubation-day."

GIRARD (G.). La réaction des nitrites pour la différenciation du bacille de la peste et du bacille de la pseudotuberculose. [**Nitrite Reaction for the Separation of the Plague Bacillus from the Bacillus of Pseudotuberculosis.**]—*C. R. Soc. Biol.* 1940. Vol. 133. No. 2. pp. 244–246.

The nitrite production by plague bacilli cultured in liver bouillon has been said to be sufficient to distinguish it from all other common organisms except the cholera vibrio. This, however, is not by any means an absolute test and is not to be compared with the rhamnose sugar test. The plague bacillus does not ferment rhamnose, whereas the pseudotuberculosis bacillus does. [See also this *Bulletin*, 1939, Vol. 36, p. 963.] *W. F. H.*

SAVINO (E.), MORALES VILLAZON (N.) & ANCHEZAR (B.). Presencia de *Pasteurella sp. incert.* en ratas grises. Importancia para el diagnostico de la peste. [**Presence of an Unidentified Species of Pasteurella in Grey Rats. Importance for the Diagnosis of Plague.**] —*Rev. Inst. Bacteriológ.* Buenos Aires. 1939. Dec. Vol. 9. No. 2. pp. 146–148. [11 refs.]

The material for examination was obtained from 15,000 rats and the method used was to sow the bone marrow on agar slopes and inoculate a suspension of the spleen in guineapigs. Pasteurella organisms have been isolated from these rodents, which are not *P. pestis.* An interesting point which emerged from the investigation was that while the bone marrow culture gave the organisms in question,

the spleen inoculation did not. It may be concluded that it is not safe to diagnose plague in rats without putting the organism isolated to a complete cultural test for *P. pestis.* *W. F. H.*

SUÁREZ (Pablo Arturo). La peste en la provincia del Chimborazo. [**Plague in Chimborazo.**]—*Bol. Oficina Sanitaria Panamericana.* 1939. Nov. Vol. 18. No. 11. pp. 1072–1078.

It was the sudden outbreak of plague in Riobamba, a town in the Andes region of Ecuador, when 16 cases of pneumonic plague made their appearance within a week, that led to special investigation of the circumstances of the outbreak. The argument developed is that in these sparsely populated regions both the rat and the flea ordinarily concerned in the transmission of plague to man are wanting. Yet plague is endemic, and epidemic outbursts, sometimes characterized by throat symptoms, make periodic appearance. In his search for possible explanation of this occurrence and in the belief that inter-human transmission of plague would account for it, the author has examined several cases of individuals in contact with plague cases. He has been able to recognize the plague bacillus in smears from the throat, while subsequent cultivation and inoculation have brought further proof of the identification of the organism. A natural deduction from the findings made is that in populations where such latent human cases exist the prophylactic measures called for should entail special examination for, and treatment of, these human carriers.

*W. F. H.*

SÁENZ (Vera C.). Brote de peste en la provincia de Riobamba, Ecuador. [**Epidemic of Plague in Riobamba, Ecuador.**]—*Bol. Oficina Sanitaria Panamericana.* 1940. Jan. Vol. 19. No. 1. pp. 40–43.

This epidemic has already been referred to [see SUAREZ above] where interhuman infection was mainly stressed. In the present article it is sylvatic plague among the guineapig type of rodents which receives most attention and a rural antiplague campaign which is advocated. It is well recognized that such a measure would be exceedingly difficult ; the people would resent a general slaughter of the guineapig rodents. But if the contention is accepted that this rodent is really the main cause of periodic epidemic outbreaks, there seems to be no other remedy for the existing state of affairs than its extermination.

*W. F. H.*

DE LA BARRERA (J. M.). Contribución al conocimiento de la peste selvática en la Argentina. Caracteres del brote de Mendoza en 1937. [**Sylvatic Plague and an Epidemic in Mendoza.**]—*Rev. Inst. Bacteriológ.* Buenos Aires. 1939. July. Vol. 8. No. 5. pp. 431–454. With 9 figs., 1 plan, 1 map & 1 coloured plate.

Mendoza is a province in the Argentine and has its problem of sylvatic plague to deal with. In the present instance a human case of septicaemic plague terminated in pneumonia and was followed by eight other cases of direct infection. The plague bacillus was isolated from the wild rodents of the district. These were : cuis of the genera Microcavia and Galea, *Graomys griseoflavus, Mus musculus* and *Lepus*

*europaeus*. It is considered probable that here, as elsewhere, the original infection of the wild rodents came from the domestic rat and that epizootics in the former slumber on, after subsidence, as enzootics. The fleas of these rodents, Parapsyllus and Rhopallopsyllus have been shown capable of transmitting plague to man. *W. F. H.*

BOLETIN SANITARIO. Buenos Aires. 1939. May. Vol. 3. No. 5. pp. 405–416. With 4 figs.—Sesion de la Comision de Asesoramiento Tecnico de la Peste. [**Meeting of the Plague Technical Council.**]

An outbreak of human plague in the Argentine province of Salta led to the discovery of extensive sylvatic plague in the Argentine-Bolivian frontier. The rodent concerned was of the genus *Sylvilagus*. Among some of the sparse populations affected it is difficult, for geographical reasons, to ascribe the entire rôle of development of human plague to an epizootic among rats. There is no doubt, however, that the domestic rat is a major factor, contracting plague through its habit of feeding on dead animals (necrophagy) at the outskirts of human habitations. The mortality among wild rodents in the case of the present epidemic had been observed and the rat gets its plague and renews its epizootics from the former. But man may get plague directly, although seldom, from the wild rodent. Thus both man and the rat represent " test " animals, in these districts, of the existence of sylvatic plague. *W. F. H.*

MEYER (Karl F.). **Sylvatic Plague.**—*Amer. Jl. Public Health.* 1939. Nov. Vol. 29. No. 11. pp. 1225–1230.

This publication is by the Chairman of the Sylvatic Plague Committee of the Western Branch American Public Health Association and is the fourth report. A previous report has already been noticed [this *Bulletin*, 1938, Vol. 35, p. 201]. New States and new countries are added to those previously reported as showing plague infection of wild rodents. The new States are Wyoming and New Mexico, as given in a table recording observations up to June 30th, 1939. Once more it is observed that " the collection and inoculation of guineapigs with pools of fleas, lice and ticks has again yielded more information than the examination of the carcases of rodents shot or trapped." The opening statement of the report is that " The Executive Committee has held no meetings. No problems were submitted for consideration. In fact, it is apparent that without further more accurate knowledge relative to the epidemiology of plague infection in rodents, no more significant and effective suppressive measures than those in use can be devised."

*W. F. H.*

MACCHIAVELLO (Atilio). Estudios sobre peste bubonica. I.—Epidemiologia de la peste Chilena. **Epidemiology of Plague in Chile.**]—*Rev. Chilena de Hig. y Med. Preventiva.* 1937. Jan.–Dec. Vol. 1. No. 1. pp. 69–87. [67 refs.]

Rat plague has existed in Chile from 1903 to 1932 and the last human epidemic took place in 1930. An analysis of epidemics of past years shows that, once started, an epidemic flares up and is followed in succeeding years by epidemics of less and less intensity until, in

some localities, there is complete disappearance. The epidemic, however, in its acute form reappears again and the same subsequent annual decrease takes place. The rat plays the preponderant rôle as reservoir in interepidemic periods and may also carry the infection from one locality to another. But this does not explain the recurrence, in cycles, of acute epidemics. The author comes to the conclusion—in confirmation of the work of LONG in Peru—that it is due to a reintroduction into the country. The vector in this reintroduction is the plague flea, brought to ports in bales of jute from India. A murine epizootic is started and then the human epidemic.

*W. F. H.*

MACCHIAVELLO (Atilio). Estudios sobre la peste bubónica. II.—Anatomia patológica de la peste murina en Antofagasta. [**Pathology of Rat Plague in Antofagasta.**]—*Rev. Chilena de Hig. y Med. Preventiva.* 1939. Jan.–Mar. Vol. 2. No. 1–3. pp. 47–52. [13 refs.]

An analysis is made by the author of 18,154 rat autopsies out of a total of 25,000, with reference to plague infection. He divides the relative classes into suspicious 2,763, very suspicious 236 and definite 88. The lesions which led to the suspicion of plague were subcutaneous injection, and any visceral or bubonic lesion. Of the visceral lesions those which were noted were found in lung, liver and spleen. Among the 88 cases definitely proved plague by isolation of the plague bacillus there were 5 acute, 64 chronic or subacute, and 19 cases where, although lesions were absent, the bacteriological examination was positive.

*W. F. H.*

LIU (C. Y.). **The Fleas of China. Order Siphonaptera.**—*Philippine Jl. Sci.* 1939. Sept. Vol. 70. No. 1. pp. 1–122. With 132 figs. [128 refs.]

ROSIER (H. J.). Verslag betreffende de pestbestrijding op Java over het jaar 1938. [**Report on the Campaign against Plague in Java in 1938.**]—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1939. Vol. 28. No. 2/3. pp. 208–281. With 13 graphs & 8 maps. English summary p. 256.

"The total incidence of plague in Java during the year 1938 was 2,107 cases with 2,083 deaths, distributed as follows: in West-Java 1,471 cases, Mid-Java 616 and East-Java 20 cases. The epidemic has diminished both in extent and in severity. For a number of years the Priangan Regencies of West-Java have formed the main focus.

"Although the plague epidemic is essentially bubonic, 202 cases of primary pneumonic plague occurred as the result of many widely spread single transmissions together with a few small group infections. Only one real outbreak of primary pneumonic plague has been recorded which claimed 48 victims in the residency of Cheribon.

"Inoculation on a large scale has been continued successfully with the living vaccine of Otten. In 1938, 1,292,257 vaccinations, mainly re-vaccinations, were given. The total number during the period 1935–1938 inclusive is 7,430,299.

"In the meantime house-remodelling as an anti-rat measure was carried on. The campaign in 1938 was an active one, the quotum of this year being 56,265 houses, by which the total number has been brought up to 1,525,364.

"Moreover 54,548 new houses have been built in this year under the supervision of the plague preventive service."

SOERONO. Vrijwillige woningverbetering in het onderdistrict Madja (Regentschap Madjalengka), Residentie Cheribon. [**Voluntary House Improvement in Madja as an Antiplague Measure.**]—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1939. Vol. 28. No. 4. pp. 283–305. With 4 graphs & 1 map.

Systematic house improvement for the indigenous population as an antiplague measure has been officially adopted by the Netherlands Government in Java since 1914, when the first legislation was passed to make the measure compulsory. That procedure has had marked success and is economical in the long run, but costly to begin with and possibly unpopular. The case of Madja, a district of the Regency of Madjalengka in the Cheribon Residency bordering on the province of mid-Java is offered, along with other districts of the Regency as an example. In this district of Madja the principle of voluntary house improvement was adopted. No compulsion was exercised except, perhaps, the indirect compulsion of strenuous official propaganda. The result may be claimed a complete success, as judged by the object attained, a total disappearance of plague and a contented population. No bonus and no official advances were offered to the people for the betterment. All the inducement held out, except that of manifest self advantage, was a premium of 3 florins for a completely reconditioned house. Why then should not the procedure adopted in this district be adopted elsewhere? There seems to be no answer but one to the question and that is: Madja as a district was specially favoured for this campaign. A voluntary method is apt to be slow in comparison with official compulsion and therefore may defeat its object. In Madja it was not slow: the people were well-to-do; compulsory methods of inspection, condemnation of houses, spleen puncture after death in suspected cases and isolation of contacts were unpopular; materials such as wood, bamboo and tiles were abundant in the district; technical advice was fully available; road communications were good. These and other factors, and especially the energy of the officials concerned, were doubtless responsible for making of Madja a model district. Details are given of procedure. A total number of houses amounting to 8,070 in February 1935 were due for improvement. In 1936 only 3 per cent. had been reconditioned; by 1937, 80 per cent. and by 1938, 97 per cent. At the end of March 1939, there remained a mere 0·38 per cent. of houses which had not been improved. It is fully recognized that such a success could not be so swiftly accomplished everywhere. The example of Madja, however, is, at least, an encouragement for the application of the voluntary as against a compulsory principle, where co-operation between government and the people can be obtained. *W. F. H.*

SAVINO (E.) & ANCHEZAR (B.). Vacunación antipestosa experimental con bacterias vivas. [**Experimental Vaccination with Living Plague Vaccine.**]—*Rev. Inst. Bacteriológ.* Buenos Aires. 1939. Dec. Vol. 9. No. 2. pp. 122–141. With 6 figs. [31 refs.]

The attenuated strains of plague known as E.V. and Tjiwidej were used to vaccinate guineapigs which were then tested by inoculation of virulent plague. In the course of vaccination about 30 per cent. of the animals die and continue to die after being inoculated with virulent plague without, however, showing plague infection. The remainder survive the test inoculation and thus demonstrate the

existence of a very solid immunity. The two strains used for immunizing give rise to the formation of a nodule in the subcutaneous tissue, whereas avirulent but non-immunizing strains produce no such nodule. The E.V. strain on intraperitoneal inoculation gives rise to granulations in the spleen, while the Tjiwidej strain does not and the former strain is superior in immunizing power to the latter [see also this *Bulletin*, 1939, Vol. 36, p. 313]. *W. F. H.*

SOKHEY (S. S.), CHITRE (G. D.) & GOKHALE (S. K.). **The Relative Value of Some Proprietary Cyanide Preparations for the Extermination of Rats and Fleas as a Plague-Preventive Measure.**—*Indian Jl. Med. Res.* 1939. Oct. Vol. 27. No. 2. pp. 389–407. With 1 diagram.

The introductory remarks to this article probably have a wider application than to the case of India alone. The authors state :—"Rat proofing of dwellings and building suitable godowns for the storage of grain is not economically possible in India, more so as the disease has become almost entirely a rural problem. Poison baiting and trapping . . . . are not very successful . . . . The usual methods of dealing with fleas in dwellings by sprinkling emulsion of kerosene oil or pesterine are even less successful. Fumigation with hydrocyanic acid gas has always proved to be the most effective method of dealing with both rats and fleas but . . . . was dangerous . . . . With the availability of new proprietary cyanide compounds . . . .fumigation of dwellings became a practical proposition." Under the conditions of testing employed one of the preparations "calcid briquettes," appears to have been eminently satisfactory—yielding its total theoretical content of hydrocyanic acid, evolving the gas with rapidity so as quickly to reach a lethal concentration, being furnished in an easily measurable form and being provided with an effective type of blower. *W. F. H.*

YOKOYAMA (Tamon). Mikrobiologische Studien ueber die Unterdrueckung der die pest Uebertragen den Tiere in der Mandschurei. [**Microbiological Studies on the Suppression of Animal Vectors of Plague in Manchuria.**]—*Jl. Oriental Med.* 1939. Sept. Vol. 31. No. 3. [In Japanese pp. 417–565. With 1 fig. & 50 charts. [234 refs.] German summary pp. 38–40.]

The ground squirrel, Citellus, is numerous and plays the chief part in the transmission of plague in Manchuria. *R. rattus* is rare and the Tarabagan is not found in that country. Experiments were conducted by the author with various strains of Salmonella for their infectivity on Citellus and *R. norvegicus*. He found that the strains Danysz, Ratin 2 and Saba-Geru were potent in infecting the former, Danysz, Ratin 2 and Hata 4 against the latter. Great care has to be exercised in the use of these various organisms in destroying plague rodents by infection lest infection of man is also caused. *W. F. H.*

DANZEL (L.). L'activité raticide de la scille maritime rouge. [**Red Scilla as a Raticide.**]—*Ann. d'Hyg. Pub., Indust. et Sociale.* 1939. Sept. Vol. 17. No. 9. pp. 381–395. With 1 fig.

The advantage of red Scilla is that it has almost a selective action. "Red Scilla kills the rat and the rat alone." Its specific botanical

name is *Urginea scilla* and it grows in the Mediterranean region. The white Scilla has no raticide power. Presumably the active principle is a glucoside but this has not been very definitely determined, although it ought to be if the powder is to be standardized and come into use for killing rats. *W. F. H.*

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## PELLAGRA.

### *Précis* of Abstracts in this Section.

Greenfield and Holmes (p. 430) report pellagra in a boy in England who lived under the same good conditions as other, unaffected, members of the family. After death (from bronchopneumonia) the post mortem findings were those of chronic gastritis and degeneration of somatic efferent neurones.

Aykroyd *et al.* (p. 431) describe the condition of angular stomatitis with glossitis and anterior stomatitis, which may be associated with various skin lesions. These lesions were observed in pellagrins some years ago by Stannus, and the authors show that nicotinic acid appears to have a curative action. Trowell (p. 431) describes the condition of pigmented dermatitis with cracking and desquamation, mental irritabilility and diarrhoea, with oedema, seen in children in Uganda, and considers it to be of pellagrous origin and also allied to nutritional oedema associated with diet deficient in protein. Moore (p. 432) in Nigeria describes the condition of retrobulbar neuritis associated with mouth and skin lesions and mental disturbance, which responds to treatment with marmite or yeast even after autoclaving.

Plunkett (p. 432) describes five cases of suspected pellagra in Cyprus but Stannus points out certain objections to this diagnosis.

Mainzer (p. 433) discusses the relatively slow rise in blood sugar in pellagrins after the injection of adrenalin. He (p. 434) considers the accentuated and prolonged fall in blood sugar following subcutaneous insulin in pellagra to be a specific reaction associated with hypoadrenalism, and that the latter hinders the normal absorption of nicotinic acid.

Meiklejohn and Kark (p. 434) consider that in the B.E.S. test of urine it is not porphyrin-like substances but indol derivatives which give the reaction.

Querido *et al.* (p. 434) have devised a method, depending upon the fact that the only growth factor required by Proteus is nicotinamide, for estimating this substance in the blood. Ritsert (p. 435) gives the amounts of nicotinic acid found in urine, blood and various tissues. Ballif *et al.* (p. 435) found normal nicotinamide content in the blood of a series of pellagrins, and conclude that the part played by nicotinic acid is as yet not understood. Lwoff *et al.* (p. 435) found low nicotinamide content in the blood of 15 of 21 pregnant women. Ballif *et al.* (p. 436) found low values of vitamin C in the cerebrospinal fluid of pellagrins and controls living on a poor diet, but Stannus in comment points out that there is no evidence that partial C deficiency plays a part in the pathogeny of pellagra.

Sal[illegible] postulates a relative insufficiency of nicotinic acid on overdosing with vitamin $B_1$ or C. Alport *et al.* (p. 437) consider that infestation with intestinal worms interferes with the absorption of vitamins, but Stannus criticizes the experiments quoted.

SYDENSTRICKER *et al.* (p. 437) found that an extract of human pellagrous liver had no curative action in pellagra, though efficient in pernicious anaemia. Commercial liver extract on the other hand was active in pellagra. Nicotinic acid does not appear to be the only factor in treatment and causation of the disease. SEBRELL and BUTLER (p. 438) conclude from experiments that the syndrome known as pellagra *sine* pellagra is due to riboflavin deficiency and suggest that pellagra may be a mixture of symptoms of deficiency in nicotinic acid, riboflavin and thiamin. JOLLIFFE *et al.* (p. 438) describe the symptoms of riboflavin deficiency. SYDENSTRICKER *et al.* (p. 439) record success in the treatment of cheilitis (thought to be due to deficiency in riboflavin) associated with pellagra, by the administration of riboflavin.

On the assumption that patients suffering from gastrogenic neurasthenia are actually sub-pellagrous, MINDUS (p. 439) obtained considerable improvement by giving a stomach extract and vitamins $B_1$ and $B_2$ together with extra meat and eggs.

FIELD and ROBINSON (p. 440) show that nicotinic acid amide, being a normal constituent of the blood, can be given in doses up to 500 mgm. without the unpleasant effects sometimes experienced after nicotinic acid. KOOSER and BLANKENHORN (p. 440) report favourably on treatment with nicotinic acid in America but GRECU *et al.* (p. 441) in Rumania have failed to obtain comparable results, and are led to conclude that the clinical picture and pathogeny of the disease in the two countries may be different. HOU (p. 441) in Shanghai shows that when oedema is present it is necessary to give increased protein as well as nicotinic acid.

Mention is made by several authors (CLECKLEY *et al.* p. 442, SALM p. 442, LIVESCO p. 442, SALEKAN p. 443) of the good effects of nicotinic acid or the amide on the mental state of patients, in some of whom this may be the only sign of pellagra. FROSTIG and SPIES (p. 443) have analysed the mental changes in cases of pellagra in relapse, largely consisting of hypersensitivity to and dislike of sensory stimuli. Intravenous cocarboxylase or vitamin $B_1$ were rapidly beneficial, nicotinic acid more slowly.

KATZENELLENBOGEN (p. 444) reports success in the treatment of epidemic glossitis with nicotinic acid and considers the condition to be due to deficiency in that substance. VILTER and SPIES (p. 444) report dramatic relief of glossitis and mental symptoms in seven patients after treatment with quinolinic acid and discuss the implications of their findings. BILLS *et al.* (p. 445) report some success with pyrazine.

IONESCU *et al.* (p. 446) failed to effect improvement with histidine. BANDIER (p. 446) successfully treated a series of patients with stomach preparations and discusses the nature of vitamin $B_2$. SPIES (p. 447) has successfully treated patients with various eye symptoms with vitamin A. *C. W.*

SPIES (Tom D.), VILTER (Richard W.) & ASHE (William F.). **Pellagra, Beriberi and Riboflavin Deficiency in Human Beings. Diagnosis and Treatment.**—*Jl. Amer. Med. Assoc.* 1939. Sept. 2. Vol. 113. No. 10. pp. 931–937. [23 refs.]

A lecture delivered at the 90th Annual Session of the American Medical Association, St. Louis, giving a very useful summary of the more recent investigations by Spies and his co-workers in pellagra

and some other associated deficiency states. This address covers ground which has already been dealt with in a number of papers each of which has been summarized in this *Bulletin*. *H. S. Stannus.*

CASTEX (Mariano R.), CAMPONOVO (Luis E.) & BORDA (Julio M.). Pelagra. [**Pellagra.**]—*Prensa Méd. Argentina.* 1940. Feb. 14. Vol. 27. No. 7. pp. 333–353. With 7 figs. [94 refs.]

i. GREENFIELD (J. G.) & HOLMES (J. MacDonald). **A Case of Pellagra. The Pathological Changes in the Spinal Cord.**—*Brit. Med. Jl.* 1939. Apr. 22. pp. 815–819. With 4 figs. on special plate. [25 refs.]

ii. STANNUS (Hugh S.). **Pellagra.** [Correspondence.]—*Ibid.* May 6. p. 950.

i. In this very interesting article brief reference is first made to the case of a 35-year-old farm labourer who came under observation for a short time in Staffordshire with mild dermal, intestinal, mental and neurological symptoms of pellagra and then a detailed case report is given of a 5-year-old boy admitted to the Staffordshire General Infirmary on 4th July, 1937, suffering from the disease. There were 5 other children in the family—boys aged 11 and 13, girls aged 7, 14 and 17 years, all of whom were well. The whole family lived under the same conditions with an excellent mixed diet. In May 1936 the patient had had typically distributed skin lesions which had cleared up in September to reappear in June 1937. The case was a most typical one in regard to affection of skin, scrotum, perineum, mouth, lips and tongue associated with looseness of the bowels, mental and nervous symptoms. Except for complete achlorhydria with no response to histamine, pathological investigations revealed nothing of note. Treatment consisted in giving six drachms of yeast per day; 4 cc. campolon were given on 15th and 22nd July. Within two weeks there was marked improvement; the child had lost his drowsiness, he could raise himself and stand once more, the mental condition was much better and he could talk; the skin had healed.

On 26th July he developed measles and died two days later of bronchopneumonia. Post mortem examination, apart from the bronchopneumonia, revealed nothing of interest except signs of a chronic gastritis—the "état mamelonné."

The report on the histological examination is full and of great interest. "The condition in the nervous system was one of neuronal degeneration in which somatic efferent neurons both upper and lower and the neurons which have their cell station in the dorsal root ganglia were chiefly affected," with some degeneration in the spino-cerebellar tracts. There was severe involvement of the basal ganglia and motor cortex and changes less intense in other parts of the cortex. The full account should be read by all interested in pellagra.

ii. In this letter attention is drawn to some among many points of interest in the case above mentioned; the close resemblance of one case to another among children; the fact that many more cases of pellagra occur in this country than are published; the selective incidence of pellagra in a family living under the same conditions—suggesting the intervention of some unknown factor; the paucity of

post-mortem findings in uncomplicated pellagra; the difficulty of correlating the neuro-histological changes with symptoms met with during life. *H. S. S.*

STANNUS (Hugh S.). **Pellagra.**—*Lancet.* 1940. Feb. 24. pp. 352–355. [45 refs.]

AYKROYD (W. R.), KRISHNAN (B. G.) & PASSMORE (R.). **Stomatitis of Dietary Origin.**—*Lancet.* 1939. Oct. 14. pp. 825–828. [19 refs.]

Nearly thirty years ago the reviewer drew attention to a condition noted among native African pellagrins for which he used the term "angular stomatitis." The condition has since become well recognized both as a sign in pellagra and as a sign associated with one or more pellagrous symptoms but without the typical skin condition, forming a number of syndromes which the reviewer collected together for discussion in 1936. Among these conditions was one described by the authors, common in Indians of the poorer classes living on a diet largely composed of rice and deficient in milk and vegetables, in which the lesions at the angles of the mouth were associated with a glossitis and an anterior stomatitis. Excoriations at the palpebral angles and in the region of the alae of the nose, erosion of the mucocutaneous [*sic*] junctions of the prepuce, anus and vagina and eczema of the scrotum may also develop—again all signs first described by the reviewer as noted in pellagrins.

The condition was originally believed by the authors to be due to a vitamin A deficiency. Later, based upon the observation that the stomatitis was cured or improved by the administration of alkaline autoclaved yeast, it was concluded that "the antistomatitis vitamin is probably identical with the factor in the vitamin $B_2$ complex which is effective in treating human pellagra."

Recently in America angular stomatitis has been written down as a symptom due to riboflavin deficiency and one which does not respond to treatment with nicotinic acid. Aykroyd points out that their good results were obtained with alkaline autoclaved yeast in which the flavin present was presumably destroyed.

In the present investigation the effect of nicotinic acid therapy was tried in these Indian cases. Fifty mgm. nicotinic acid was given daily to each of 14 patients for 26 days. Four greatly improved, 5 showed some improvement, 5 remained unchanged. Among 9 controls untreated 3 showed slight improvement, 5 remained unchanged, 1 became worse. These results, it is stated, suggest that a nicotinic acid deficiency is concerned in the causation of these cases of stomatitis. In most cases the glossitis immediately improved. The problem, as the authors state, needs much further clarification. *H. S. S.*

TROWELL (H. C.). **Infantile Pellagra.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1940. Jan. 29. Vol. 33. No. 4. pp. 389–404. With 4 figs. (3 on 2 plates). [76 refs.]

This article, itself a review of the published communications on the subject, is a little difficult to summarize. It will be read by all those who may meet with similar conditions in tropical native races with interest. A large number of the earlier observations, beginning with those of R. A. W. PROCTOR (1926) in Kenya, came from Africa and

included those of C. WILLIAMS (1933) and R. U. GILLAN (1934). These were collected together by H. S. STANNUS (1936) [this *Bulletin*, 1936, Vol. 33, p. 729] who pointed out that they referred to a condition which must be recognized as pellagrous. The following year H. C. Trowell again reviewed these cases in Africa, but in the present paper he deals with the condition as it has been reported not only from East and West Africa but also from Congo, Central America, the United States and elsewhere. The essential features of the affection are the occurrence of deeply pigmented patches of dermatitis with cracking and desquamation on the limbs and elsewhere, mental irritability, diarrhoea, etc., together with oedema of face and extremities or more widespread.

The clinical picture in various groups of cases varies somewhat, suggesting a deficiency of more than one dietetic factor. While confirming the essentially pellagrous nature of the condition Trowell believes that the oedema is probably allied to " nutritional oedema " associated with a diet deficient in protein. *H. S. S.*

MOORE (D. Fitzgerald). **Retrobulbar Neuritis & Pellagra in Nigeria.**—*Jl. Trop. Med. & Hyg.* 1939. Apr. 15. Vol. 42. No. 8. pp. 109–114. With 5 figs. [16 refs.]

Among the many conditions which have been recorded among native races in various parts of the world [see this *Bulletin*, 1936, Vol. 33, p. 885] as due to dietetic deficiencies, one of the most interesting is that originally described by Dr. FITZGERALD-MOORE in 1934 [this *Bulletin*, 1934, Vol. 31, p. 820].

In the present article the author brings his observations up to date. The syndrome with which he deals consists essentially in a retrobulbar neuritis associated with soreness of the tongue, angular stomatitis, a dry scaly condition of the skin of the genitalia and areas subjected to pressure, together with mild mental changes and " burning feet." The affection is found among the unemployed, pregnant mothers in poor circumstances, immigrant town labourers and above all among the boarders of schools in which the diet is poor.

It responds to treatment with marmite, dried brewer's yeast and the same products after being autoclaved, the skin and mouth lesions clearing up in a few weeks, the visual defects in 3 or 4 months provided the disease has not existed too long. Unfortunately it was not possible to carry out a fair trial of nicotinic acid in these cases. Reference is made to the observations of others concerning retrobulbar neuritis in pellagra and reasons are given for believing that this condition in West Africa is pellagrous.

In the latter part of his article the author discusses food supplies of these natives and food in relation to income and alludes to some general principles underlying a sound policy in regard to nutrition. Reference is also made to the possibility that manioc (gari) plays some part as a toxic element in the dietary. *H. S. S.*

PLUNKETT (O. R. L. L.). **Observations and Clinical Notes on Some Cases of Pellagra seen in Cyprus.**—*Jl. Roy. Army Med. Corps.* 1939. May. Vol. 72. No. 5. pp. 317–327. With 5 figs.

Two cases diagnosed as pellagra, one of probable pellagra and two others in which the condition was thought to be pellagra *sine* pellagra

are reported, making five in all—five out of nine wives on a military station; four were wives of sergeants, one the wife of a captain, R.A.M.C.

The case histories are not very full and no clinico-pathological investigations were possible.

The diagnosis in the first two cases depended on the appearance of a rash on the skin of exposed parts, a red and puffy face with some loss of appetite, listlessness and irritability. In the third case there was a similar rash. In the other two cases there were diarrhoea, loss of weight, sore mouth, depression and irritability but no rash. In the last of these cases there was noted the passage of very large quantities (4 oz. at a time) of mucus *per rectum*. The rash is said to have resembled closely lichen planus, though of a different colour and different distribution and the suggestion is made that lichen planus may be a form of pellagra in less sunny countries. Improvement occurred with treatment by bemax, marmite, yeast, milk and a good mixed diet. The dietary preceding the illness was considered a poor one.

[On reading this account one is left with a sense of being unconvinced. The description of the exanthem is a little odd; the mental changes were no more than are commonly met with in many affections of the skin. A mucous colitis is no part of pellagra. The deficiencies in the diet hardly sound sufficient to cause pellagra. The suggestion that lichen planus may represent pellagra in a temperate zone is made surely in ignorance of the fact that the skin lesions in temperate countries resemble exactly those occurring in the tropics.

The author makes a point of the fact that in his first case the exanthem occurred at a time when the patient had not been exposed to the sun for two months and believes this is the first time such a phenomenon has been recorded. It is an interesting observation but the subject was discussed for the first time and an explanation offered by the reviewer some years ago (this *Bulletin*, 1937, Vol. 34, p. 183).]

*H. S. S.*

MAINZER (Fritz). Ueber Pellagra. III. Mitteilung. Die Blutzuckerkurve der Pellagrakranken nach peroraler Zufuhr von Traubenzucker und nach subkutaner Gabe von Adrenalin. [**The Blood Sugar in Pellagra after Oral Glucose and Subcutaneous Adrenalin.**] —*Acta Med. Scandinavica.* 1939. Vol. 100. No. 3–5. pp. 231–243. With 2 figs.

The rise in blood sugar content after the ingestion of glucose 30 gm. is the same in pellagrins as in normal individuals, showing that in that disease there is no difficulty in glucose absorption. Among pellagrins, however, after an injection of 0·5 mgm. adrenalin this rise in blood sugar is twice as slow as among normal persons.

It will be necessary to find out whether this picture is provoked by a lack of glycogen reserves in pellagra or possibly by lesions of the sympathetic, the pituitary or thymus; in other words whether the lesion is nervous or humoral. Defective function of the adrenal glands is probably a factor, but not the only one. *H. S. S.*

MAINZER (Fritz). Ueber Pellagra. II. Mitteilung. Insulin-Ueberempfindlichkeit bei Pellagrakranken. [**Hypersensitivity to Insulin in Pellagra.**]—*Acta Med. Scandinavica.* 1939. Vol. 100. No. 3–5. pp. 208–230. With 5 figs. [31 refs.]

Injection subcutaneously of a small quantity (5 units) of insulin caused a marked reaction among nine male and seven female pellagrins, characterized by a very accentuated and prolonged fall in the blood sugar. The return to normal may be long delayed or absent. Symptoms of hypoglycaemia may persist for several days. This reaction may persist even after an apparent cure of the pellagrous condition has been established. It has been shown that the reaction is due to undernourishment from the quantitative point of view and not to lack of vitamin B.

The author considers it a specific reaction of pellagra, and believes that it is associated with an hypoadrenalism which causes an increased insulin-sensitivity. It is suggested that adrenal hypofunction also hinders the normal absorption of nicotinic acid. A vicious circle may thus be formed which would explain the liability to relapse and the impossibility of establishing cure by dietetic treatment alone. It will be necessary to find out whether a functional lesion in the adrenals can be demonstrated as a factor in the causation of pellagra.

*H. S. S.*

MEIKLEJOHN (Arnold P.) & KARK (Robert). **Pigment Excretion in Pellagra.**—*New England Jl. of Med.* 1939. Oct. 5. Vol. 221. No. 14. pp. 519–521. With 1 fig. [12 refs.]

A good deal of attention has been drawn in the last two or three years, to the excretion of pigmentary substances in the urine of pellagrins. These were at first believed to be porphyrins and later were designated, by SPIES and his associates in America, " porphyrin-like substances," in view of the positive results obtained with the B.E.S. test [see this *Bulletin,* 1939, Vol. 36, p. 547]. This test consists in extracting with 25 per cent. hydrochloric acid an acetic acid ether extract of urine.

A pink colour in the hydrochloric acid layer was considered by Spies to indicate the presence of porphyrin-like substances. In the present paper, which everyone interested in the subject will read in full, the conclusion is reached that the " positive B.E.S. test is due to the oxidation of ether soluble indol derivatives in the presence of hydrochloric acid, with the production of pigments giving a characteristic urorosein reaction," which derivatives in no way resemble porphyrin-like substances. *H. S. S.*

QUERIDO (Andries), LWOFF (André) & LATASTE (Camille). Le dosage de la nicotinamide dans le sang. [**The Estimation of Nicotinamide in the Blood.**]—*C. R. Soc. Biol.* 1939. Vol. 130. No. 14. pp. 1580–1584. With 1 chart.

Estimations of nicotinic acid in the blood by chemical methods (KARRER and KELLER, VILTER, SPIES and MATHEWS, SWAMINATHAN KRINGSTAD and NAESS) present various difficulties. Swaminathan in single estimations in three individuals, found values of 0·33, 0·37, 0·53 mgm. per 100 cc. Using the observation of FILDES who showed that the only growth factor required by Proteus was nicotinamide

(or nicotinic acid) the authors give a detailed account of a method for thus estimating this substance in human blood. The method need not be reproduced here as the original article will be consulted by all those interested. The values found varied between 0·62 and 0·89 mgm. per 100 cc. *H. S. S.*

RITSERT (K.). Zur quantitativen Nicotinsäure- und Nicotinsäureamid-Bestimmung im Harn, in Geweben und im Blut. [**The Quantitative Estimation of Nicotinic Acid and Nicotinamide in Urine, Tissues and Blood.**]—*Klin. Woch.* 1939. July 8. Vol. 18. No. 27. pp. 934–936. With 2 figs. [15 refs.]

An article detailing methods for the determination of the nicotinic acid and nicotinamide content of the urine, blood and tissue—from the chemical laboratories of Merck, Darmstadt.

The actual methods employed cannot be here summarized but the values obtained were as follows:

In urine of the healthy individual 50 to 300γ nicotinic acid per 100 cc.

In blood 330 to 460γ nicotinic acid per 100 cc.

In liver 7·85 mgm. nicotinamide in 100 gm.; in muscle 6·47 mgm. in 100 gm.

For the estimations 10–20 cc. of urine, 10 gm. of tissue, or 5 cc. of blood are used. *H. S. S.*

BALLIF (L.), LWOFF (A.), QUERIDO (A.) & ORNSTEIN (I.). La nicotinamidémie chez les pellagreux. [**Blood Nicotinamide in Pellagrins.**]—*C. R. Soc. Biol.* 1939. Vol. 131. No. 20. pp. 903–907. [12 refs.]

Many writers would appear to look upon black tongue of dogs and human pellagra as homologous and they would identify the pellagra-preventive factor with nicotinic acid. Others, however, are more cautious.

The authors, arguing that if the former be in the right pellagrins should show a low nicotinamide blood content, made estimations in the case of ten pellagrins. These cases all showed characteristic skin lesions, one had glossitis and two achlorhydria but none had any other gastro-intestinal symptoms nor mental changes. In all normal values were found for nicotinamide. They suggest that the low values which others have found may be due to loss by diarrhoea.

It is of interest to remember that the so-called pellagra gastropriva of the pig is not cured by nicotinic acid, a fact which suggests that the stomach performs some specific function in pellagra prevention [as was pointed out by the writer of this summary for the first time on epidemiological grounds—this *Bulletin*, 1937, Vol. 34, p. 183]. The authors conclude by stating their belief that the part played by nicotinic acid is still an unsolved problem. *H. S. S.*

LWOFF (A.), QUERIDO (A.), DIGONNET (L.) & GARNIER, Mlle. La nicotinamidémie chez les femmes gravides. [**Blood Nicotinamide in Pregnant Women.**]—*C. R. Soc. Biol.* 1939. Vol. 131. No. 20. pp. 900–903.

Some earlier researches carried out to determine the nicotinamide content of normal blood suggested that the mean was 0·74 mgm. per 100 cc. with upper and lower levels of 0·89 and 0·62.

More recent investigations go to show that values between 0·62 and 0·70 should be considered subnormal. The Proteus test of Fildes has been used in all cases. Believing that minor degrees of what they call P. P. avitaminosis may occur, due to deficiency in absorption or metabolism rather than due to a deficiency in the diet, they made estimations of the nicotinamide content of the blood in pregnant women who, as has been shown by others, are liable to vitamin deficiencies in other directions.

Fifteen of twenty-one pregnant women tested showed low levels—the average being 0·57 mgm. per 100 cc., the lowest value was 0·37. [In the present state of our knowledge it seems a pity to call nicotinic acid or the amide specifically the "pellagra preventive factor," the problem is not yet solved.]

*H. S. S.*

v. EULER (Hans) & SCHLENK (Fritz). Nicotinsäureamid und Co-Zymase im Blut. [**Nicotinic Acid Amide and Cozymase in the Blood.**]—*Klin. Woch.* 1939. Aug. 19. Vol. 18. No. 33. pp. 1109–1111. [21 refs.]

BALLIF (L.), NITZULESCU (J.), ORNSTEIN (I.) & BALLIF (L. E.). Sur la teneur en acide ascorbique du liquide céphalorachidien chez les pellagreux. [**The Ascorbic Acid Content of the Cerebrospinal Fluid in Pellagrins.**]—*C. R. Soc. Biol.* 1939. Vol. 130. No. 14. pp. 1595–1599.

Some have thought that a vitamin C deficiency is a factor in causation of pellagra.

The authors, working in Moldavia and using the indophenol titration method of Tillmans and Harris, have made estimations of the vitamin C content of cerebrospinal fluid in 36 cases of pellagra.

In 28 of the 36 cases values below 0·6 mgm. per 100 cc. were found; in 22 the figure was below 0·3. The same low values were, however, found in controls—cases admitted to hospitals for various nervous and mental diseases. The well-balanced diet received in hospital caused no rise in the vitamin C content of patients with low values, all of whom before admission were living on a pellagra-producing diet. On the other hand the exhibition of 500 mgm. of pure vitamin C for 5 days produced a three-fold rise in the c.s.f. content of vitamin C.

The authors found no correlation between lowered values and increasing age as described by MARINESCU. [Low contents for vitamin C must be of common occurrence among pellagrins in endemic areas judging by the dietaries in such areas. Though such populations live on the edge of a scorbutic precipice, so to speak, there is no evidence that the partial C deficiency plays a part in the pathogeny of pellagra.]

*H. S. S.*

SALVESEN (Olaf). Pellagra og pellagrøse hudforandringer efter behandling med vitamin $B_1$ og vitamin C. [**Pellagra and Pellagrous Dermatitis after Treatment with Vitamins $B_1$ and C.**]—*Nordisk Med.* 1940. Feb. 17. Vol. 5. No. 7. pp. 279–282. With 3 figs. English summary.

"A report is given of 3 cases of pellagrous dermatitis due to treatment with vitamin $B_1$ and vitamin C. In the first case is described a patient with pellagra without dermatitis, who had previously been subjected to gastroenterostomia. The diet had been sufficient in the P.P. factor. The patient grew worse during treatment with vitamin $B_1$ and yeast, and

typical pellagrous dermatitis was observed, but all the symptoms were improved during treatment with nicotinic acid. Later there was twice relapse on discontinuing nicotinic acid, and therefore he is now continually being treated with nicotinic acid.

"In the second case there was no B-avitaminosis, but the patient was over-treated with vitamin $B_1$, and during this treatment typical pellagrous dermatitis appeared, but no other symptoms of pellagra.

"The third patient developed typical pellagrous dermatitis during over-treatment with ascorbic acid.

"It may be reasonable to suppose there is relative insufficiency of nicotinic acid on over-dosing with vitamin $B_1$ or vitamin C, which are supposed to act synergically."

ALPORT (A. Cecil), GHALIOUNGUI (P.) & EL GHARINY (Abbas). **Defective Gastro-Intestinal Absorption in Pellagra.**—*Jl. Egyptian Med. Assoc.* 1939. Apr. Vol. 22. No. 4. pp. 191–197. With 2 charts. [12 refs.]

The authors are among those who believe that deficient intestinal absorption plays an important part in the causation of pellagra. The high percentage of pellagrins in Egypt exhibiting helminth infections is considered a point of importance in this relation. It was thought of interest to try to determine whether malabsorption from the intestine among pellagrins also applied to other vitamins and vitamin C was chosen for the experiment. The authors' conclusions were that pellagrins, to whom 300 mgm. ascorbic acid were given by mouth, excrete in the urine less vitamin C than normal persons. If the acid be given by injection excretion is normal.

[The pellagrins and controls each numbered 25 persons; all the pellagrins, it is stated, had worm infestations but nothing is said concerning helminth infections in the controls. The experiment seems to miss the point. There are two questions at issue—(1) Do helminth infestations of the bowel lead to malabsorption of vitamins from the intestine? (2) If this be true does such malabsorption lead to the production of pellagra? From the observations so far made neither question receives an answer.] *H. S. S.*

SYDENSTRICKER (V. P.), SCHMIDT (H. L.), Jr., GEESLIN (L. E.) & WEAVER (J. W.). **The Liver in Pellagra.**—*Amer. Jl. Med. Sci.* 1939. June. Vol. 197. No. 6. pp. 755–763. With 3 charts. [27 refs.]

Before the introduction of nicotinic acid in the treatment of pellagra good results had been obtained by the exhibition of liver extracts.

Since crude liver extracts were later found to contain nicotinic acid it was assumed that their potency depended on their nicotinic acid content. It has, however, been demonstrated that the most efficacious remedy for intravenous use is the G fraction of Cohn which owing to its method of preparation must contain no nicotinic acid though there may be present very small amounts of nicotinamide.

The authors seized the opportunity presented by the death of an advanced case of pellagra under their care, of preparing an extract by Cohn's method of human pellagrous liver. This preparation, which contained no demonstrable nicotinic acid or nicotinamide, produced a prompt and satisfactory reticulocyte response in a case of pernicious anaemia. Given in doses of 25 cc. intravenously to two pellagrins

on two successive days it caused no improvement. To these same two cases 75 mgm. of nicotinic acid were then given daily for four days by the intravenous route, again without improvement. Finally 20 cc. of a commercial liver extract were given intravenously—the result was dramatic.

The first part of the experiment is of considerable interest as it had already been shown that an extract of pernicious anaemia liver would cure pellagra. It forms the complementary proof that the pernicious anaemia factor and the pellagra-preventing factor are independent of each other.

The second part of this experimental treatment has still further interest. The therapeutics *and* causation of pellagra would appear not to be such a simple problem as was suggested when nicotinic acid was first introduced in treatment of the disease. The many resemblances to pernicious anaemia are once more called to mind. [This question was brought forward and discussed in an article dealing with the Theories of Causation of Pellagra in this *Bulletin*, 1937, Vol. 34, p. 183.] *H. S. S.*

SEBRELL (W. H.) & BUTLER (R. E.). **Riboflavin Deficiency in Man (Ariboflavinosis).**—*Public Health Rep.* 1939. Dec. 1. Vol. 54. No. 48. pp. 2121–2131. With 1 fig. [16 refs.] [Summary appears also in *Bulletin of Hygiene.*]

A diet deficient in riboflavin was given to 18 adult white women for a year, and 13 developed mucosal lesions of the lips (cheilosis), fissures in the angles of the mouth and seborrhoea at the naso-labial folds, 95 to 293 days after beginning the diet. The lesions were unaffected by the addition of nicotinic acid to the diet but disappeared when daily doses of riboflavin (1 mgm. for 3 days, followed by 0·025 mgm. per kilo. body weight daily) were given. When the riboflavin was discontinued the lesions reappeared but were again cured by riboflavin therapy. Four of 8 women, who had developed no lesions by the 139th day, were given prophylactic doses of riboflavin (0·025 mgm. per kilo. body weight) and remained free from lesions. Only 1 of the 18 women developed no lesions during the year. The authors conclude that the syndrome known as pellagra *sine* pellagra is due to riboflavin deficiency, and suggest that pellagra may be a mixture of symptoms caused by three deficiencies, *viz.*, nicotinic acid, riboflavin and thiamin ; any one may occur alone or in combination with any other.

*H. N. H. Green.*

JOLLIFFE (Norman), FEIN (Harry D.) & ROSENBLUM (Louis A.). **Riboflavin Deficiency in Man.**—*New England Jl. of Med.* 1939. Dec. 14. Vol. 221. No. 24. pp. 921–926. With 4 figs. [Summary appears also in *Bulletin of Hygiene.*]

Lesions were observed in 15 patients, similar to but more advanced than those produced in women by experimental riboflavin deficiency [SEBRELL & BUTLER, *supra*]. There were seborrhoeic excrescences usually in the naso-labial folds, but frequently on the alae nasi and less often the bridge of the nose and the forehead. The skin in these areas showed a fine, scaly, greasy desquamation, with maceration and fissures at the angles of the mouth. The epithelium of the lips, especially the lower, showed degenerative changes. These lesions

cleared up after the administration of natural (yeast or liver residue) or synthetic riboflavin. They showed no response to diets deficient in the vitamin B complex or to nicotinic acid. In one patient scorbutic lesions of the gums were cured with ascorbic acid, the oral lesions of pellagra by nicotinic acid, the filiform lesions of the face by riboflavin, and finally she was left with a peripheral neuritis which cleared after treatment with thiamin. Even then she did not gain weight and a facial acne did not improve until a vitamin-rich diet, supplemented by yeast, was given. All the cases, except one, showed lesions due to other vitamin deficiencies: pellagra, polyneuritis and scurvy, in that order, being most frequent. Several cases had lesions of two deficiency diseases in addition to those of riboflavin deficiency. Since the true nature of these lesions was recognized one case a month, with lesions of riboflavin deficiency, has been seen and it appears that, though most of the previous cases were reported from the South, it is not uncommon in the North-Eastern States of America. *H. N. H. Green.*

SYDENSTRICKER (V. P.), GEESLIN (L. E.), TEMPLETON (C. M.) & WEAVER (J. W.). **Riboflavin Deficiency in Human Subjects.**—*Jl. Amer. Med. Assoc.* 1939. Nov. 4. Vol. 113. No. 19. pp. 1697–1700. With 8 figs.

After making reference to some recent papers on the subject [all reviewed in this *Bulletin*] the authors, writing from Augusta, Ga., give notes of six cases, recently under observation, exhibiting the "cheilitis" which is thought to be due to a riboflavin deficiency. Five of the six had also signs of pellagra. In five there was response as regards the cheilitis to the exhibition of riboflavin. In Case 2 the cheilitis and rash were cured by nicotinic acid plus ample diet. In this case it is supposed the diet contained riboflavin. In Case 4 the severe cheilitis, without signs of pellagra, cleared up with riboflavin. In Case 3 in which there was conjunctivitis and what is described as an atypical dermatitis both signs disappeared under riboflavin treatment.

In three other cases the lip condition cleared quickly with riboflavin therapy but immediately relapsed when discontinued. *H. S. S.*

MINDUS (E.). Gastrogena psykoser och pellagra. [**Gastrogenic Psychoses and Pellagra.**]—*Nordisk Med.* 1939. Vol. 3. pp. 2477–2486. With 6 figs. [49 refs.] English summary.

At the Beckomberga Mental Hospital in Sweden where, during the past two years, five well-defined cases and many ill-defined cases of pellagra have been observed, Mindus has supplemented the routine medical examination of the patients admitted to a woman's department with test meals and faeces examinations and, in some cases, with radiological examinations. Among 90 women thus examined were 34 found to be suffering from achylia and 48 from hypochylia. Yet hardly any of these patients had complained of dyspeptic phenomena. Wondering if many of his patients might not be suffering from pellagra in an early stage and without any cutaneous manifestations, Mindus classed his patients in two groups as they were admitted to hospital. The patients in both groups suffered from depression, with or without paranoia, but without signs of schizophrenia or manic-depressive psychoses. All the patients in both groups suffered from achylia or hypochylia, and characteristic signs

and symptoms in both groups were lassitude, anorexia, loss of weight, simple anaemia, insomnia, amenorrhoea, restlessness and anxiety or apathy. These patients fitted, in other words, into the clinical picture commonly labelled " gastrogenic neurasthenia." The two groups were identical except for this, that the average age of the patients was higher and the duration of the disease was somewhat longer in the first than in the second group.

While the second group served as a control, the first group was treated on the assumption that the patients in it were sub-pellagrous. They were given hydrochloric acid and a stomach extract, and some of them were also given vitamins $B_1$ and $B_2$. Extra rations of meat and eggs were also provided. The patients in the second group were given the routine treatment with sedatives, etc., but they received no extra supply of vitamins and were given no stomach extract. This experiment having been carried out in the autumn of 1937, ELVEHJELM's discovery of the action of nicotinic acid was not yet known and could not, therefore, be exploited. The two groups were compared by two assessors one of whom did not know to which group each of the patients he examined belonged. They were classified according as they had recovered, had improved, or had not improved. Thus judged, the patients in the first group fared on the whole considerably better than those in the second group. *C. Lillingston.*

FIELD (Henry), Jr. & ROBINSON (William D.). **The Absence of Reactions following Therapeutic Doses of Nicotinic Acid Amide.**—*Amer. Jl. Med. Sci.* 1940. Feb. Vol. 199. No. 2. pp. 275–276. [17 refs.]

Since nicotinic acid amide is a normal constituent of the body while nicotinic acid is not, it might have been expected that though the latter produced definitely unpleasant symptoms when administered to man the former would not do so. This of course is known to be the case. The fact is confirmed by the author who shows that up to 500 mgm. doses of the amide may be given on an empty stomach without causing any vasodilatation or any abdominal, cerebral or cardiac symptoms. *H. S. S.*

KOOSER (John H.) & BLANKENHORN (M. A.). **Pellagra of Kentucky Mountain Folk : Ambulatory Treatment with Nicotinic Acid.**—*Jl. Amer. Med. Assoc.* 1939. June 24. Vol. 112. No. 25. pp. 2581–2584.

During the period 15th May to 1st November, 1938, an attempt was made to treat at an outpatient clinic such cases of pellagra as were thereto referred. Their number was 41—5 males and 36 females, many of whom were pregnant. They came from a mountain folk employed in coal mining who no longer farm the land but live for the main part on syrup, cornmeal and fat meat. Pellagra has long been endemic there. Of the 41 patients, 24 had had 1 to 10 previous attacks, 17 were in the initial attack.

Treatment consisted in giving a week's supply of tablets of nicotinic acid. 150–200 mgm. daily was the dose in most cases but 800 mgm. or more were occasionally necessary. Treatment was carried on for 3 weeks. All patients improved but in only 28 was complete relief of symptoms seen, in the remainder a good deal of ill-health persisted.

The symptoms in the 41 cases besides the dermatitis were diarrhoea in 15, constipation 6, anorexia 29, loss of weight 19, glossitis 22, stomatitis 8, vaginitis 3. *H. S. S.*

GRECU (Aurel), IONESCU (N. Gruia), CLAUDIAN (I.) & CONSTANTINESCU (P.). Contributions au traitement de la pellagre en Roumanie par l'acide nicotinique. [**Treatment of Pellagra with Nicotinic Acid.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Bucarest.* 1939. Nov.–Dec. Vol. 21. No. 9–10. pp. 493–504. [47 refs.]

In a previous communication these authors, on a basis of 18 cases of pellagra treated with nicotinic acid, found that their results were in no way comparable with those obtained by American observers [see this *Bulletin*, 1939, Vol. 36, p. 552].

The present article gives their further results in an attempt to evaluate treatment by nicotinic acid and nicotinamide. The 50 cases studied were divided into three groups and details of each are given in the form of tables with analyses. The first group received the ordinary hospital diet, the second one containing no pellagra-preventive factor, the third received a diet as in the first but were treated by "hygieno-dietetic means and usual medicines" for a preliminary period. The specific treatment consisted in the administration of nicotinic acid or its amide in doses of 100–800 mgm. per day for periods varying from 2 to 26 days—the total quantity being from 1·4 to 3·6 gm.

The results in group 2 were worse than in group 1. Of those in group 3 two-thirds improved under non-specific treatment and those that did not so improve remain uninfluenced by nicotinic acid. The authors reach the conclusion that nicotinic acid appears to be an adjuvant of a certain value in treatment but difficult to estimate. The dosage remains an unsettled question. The amide appears to be more active than nicotinic acid. Lastly, they think that the clinical picture of pellagra in Rumania may differ from that in the United States and that there may be differences in pathogeny in the two countries. *H. S. S.*

HOU (H. C.). **Pellagra and its Treatment with Nicotinic Acid.**—*Chinese Med. Jl.* 1939. June. Vol. 55. No. 6. pp. 528–536. With 4 figs.

Some notes upon six cases of pellagra, of fairly mild type, met with at the Institute of Medical Research Hospital, Shanghai, in August and September 1938, four of which were treated with nicotinic acid and two with yeast. Five were males, one a female; all had been living on a diet which appeared to be deficient in vitamin $B_2$. All yielded satisfactorily to treatment. One showed signs of vitamin $B_1$ deficiency and was treated with that vitamin. Others showed oedema which did not clear up until the protein content of the diet had been increased. *H. S. S.*

DAVIS (J. Preston). **The Symptoms, Diagnosis and Treatment of Pellagra with Special Reference to the Use of Nicotinic Acid.**—*New Orleans Med. & Surg. Jl.* 1939. Dec. Vol. 92. No. 6. pp. 315–320.

ROBERTSON (Douglas S.). **Nicotinic Acid Treatment of Pellagra. With Report of a Case occurring in Edinburgh.**—*Edinburgh Med. Jl.* 1940. Feb. Vol. 47. No. 2. pp. 81–85.

CLECKLEY (H. M.), SYDENSTRICKER (V. P.) & GEESLIN (L. E.). **Nicotinic Acid in the Treatment of Atypical Psychotic States associated with Malnutrition.**—*Jl. Amer. Med. Assoc.* 1939. May 27. Vol. 112. No. 21. pp. 2107–2110.

Nineteen patients with no history or symptoms of pellagra in the generally accepted sense but exhibiting mental changes characterized by stupor associated with glossitis were submitted to treatment with nicotinic acid.

The patients were in all cases older people and all had organic disease, mostly arteriosclerosis. They had all suffered a period of chronic inadequate nutrition. Glossitis was present in all but two. In one only was stomatitis found. In two vaginitis was present; in none diarrhoea or skin lesions.

The nicotinic acid, except in one case, was administered intravenously as sodium nicotinate in doses of 100 to 300 mgm. daily for 3–10 days.

In 4 cases there was great improvement, in 15 " cure " was dramatic.

In view of the therapeutic reaction to nicotinic acid these cases must be diagnosed as pellagra and the conclusion is arrived at that " cerebral " (mental) symptoms may be the earliest symptoms of a nicotinic acid depletion. *H. S. S.*

SALM (H.). Eine Pellagraerkrankung im bayrischen Schwaben, deren körperlichen und geistigen Störungen durch Nikotinsäureamid (Merck) geheilt wurden. [**Physical and Mental Disturbances of Pellagra cured by Nicotinic Acid in Bavaria.**]—*Muench. Med. Woch.* 1939. June 9. Vol. 86. No. 23. pp. 882–884. [16 refs.]

Most of the cases of pellagra in Germany are met with in mental institutions, 84 per cent. of them being women. In the present article the case of a 38-year-old woman is described from Munich. She was transferred to a mental institution from hospital whither she had been admitted undiagnosed from very poor and dirty surroundings. She had lived on bread, potatoes, and a few vegetables. The case, as far as the description goes, was a typical one of chronic pellagra in a late stage—rash, digestive disturbances, dementia with hallucination and suicidal tendencies, etc. Treatment by means of nicotinic acid was followed by rapid improvement; she was able to leave the mental hospital, well, after 8 weeks. *H. S. S.*

LIVESCO (M.). Le traitement de la pellagre par l'amide de l'acide nicotinique. [**The Treatment of Pellagra by Nicotinic Acid Amide.**]—*Bull. Acad. Méd. Roumanie.* 1939. 4th Year. Vol. 8. No. 5–6. pp. 439–441.

The author describes in brief three pellagrous patients with acute mental symptoms, who after having suffered for a long period and undergone various forms of treatment, showed considerable improvement in a couple of days after taking nicotinic acid amide and were able to leave hospital in 10 days or so. The history of one case will suffice; the others were very similar.

A man of 52 years had shown pellagrous symptoms for 3–4 years. Two or three weeks before admission to hospital he lost his appetite, became depressed and taciturn, and later agitated, uttering inarticulate cries and destroying clothing and surrounding objects. He suffered

also from diarrhoea and passed stools in his room regardless of conveniencies.

He was given nicotinic acid amide in "small doses" increasing rapidly to 30–40 cgm. daily. By the third day after this treatment was started he became calm and talked sensibly with those about him and asked for food. He still seemed depressed. After four days the drug was stopped. He maintained his improved state for 2–3 days and then relapsed again to delirium and agitation. Resumption of the drug was followed in two days by amelioration and administration was kept up for another 4–5 days. The improvement continued and the patient left hospital in ten days "in a normal state." Previous to this, treatment during two years by iron, arsenic, hydrochloric acid, pepsin and brewers' yeast, separately and combined, had proved ineffectual. *H. H. S.*

SALEKAN. Een geval van pellagra, behandeld met nicotinezuur. [**A Case of Pellagra treated with Nicotinic Acid.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1939. Aug. 8. Vol. 79. No. 32. pp. 2013–2016. With 2 figs. on 1 plate.

The case here recorded is that of a European woman of 40 years, in Buitenzorg. Her previous history mentioned amoebic dysentery which was treated with injections of emetine. After this she put herself on a much restricted diet, and became a vegetarian. She suffered from delusions and hypochondria; reflexes were normal. There was some degree of anaemia, red cells 5 million, haemoglobin 70 per cent., colour index 0·7; white corpuscles 8,300, with some relative lymphocytosis, 30 per cent. She presented a typical pellagra rash on face, hands and feet. She was given nicotinic acid, 5 mgm., three times a day, and in three days there was marked improvement in the local symptoms, but the psychical were becoming more manic than depressive; her general behaviour, however, was better and she was beginning to pay more attention to her surroundings. It is thought that the pellagra was brought on by her voluntarily restricted diet.

*H. H. S.*

FROSTIG (J. P.) & SPIES (T. D.). **The Initial Nervous Syndrome of Pellagra and Associated Deficiency Diseases.**—*Amer. Jl. Med. Sci.* 1940. Feb. Vol. 199. No. 2. pp. 268–274.

Mental changes are not uncommon in cases of pellagra in relapse. Sixty such cases, many of them showing an "associated beriberi and riboflavin deficiency," were selected for this special study in which an analysis of the symptoms and experiences reported by the patients has been made. It was found that the symptoms varied very little in the whole group, individual mental make-up played little or no part in determining the picture. The symptoms consist of:—hypersensibility to all forms of sensory stimuli with dislike, engendered by the hypersensibility, to noises or music, sweet smell or evil odour, etc. The smell of cooking may be absolutely intolerable; certain abnormal skin sensations—difficult to define and difficult to differentiate in regard to causation, those for instance which might be considered as subjective, from those which might be ascribed to a neuritis; restlessness, fidgetiness, sleeplessness associated with physical weakness and increased fatiguability; oversensitiveness, excitability, emotionalism, with apprehensiveness in the majority—"always on edge"; dizziness—

a very common symptom and headache which the authors hold is of true migrainous type.

Many of these cases were treated with large doses of cocarboxylase, nicotinic acid, riboflavin or synthetic vitamin $B_1$ but the results will be published later elsewhere; a note is made however that the intravenous injection of cocarboxylase or vitamin $B_1$ "produced an almost immediate reversal of the neurologic signs within a few hours." Nicotinic acid produced the same effect but more slowly. Disturbances of touch and pain and corneal reflex improved in 24 hours but not so altered tendon reflexes, nystagmus and weakened accommodation.

*H. S. S.*

MARU (A. M.). **Acute Dementia due to Pellagra treated by Nicotinic Acid.**—*Med. Bull.* Bombay. 1939. Dec. 2. Vol. 7. No. 23. pp. 740–741.

LEWY (F. H.), HIMWICH (H. E.), FROSTIG (J. P.) & SPIES (T. D.). **The Effect of Cocarboxylase upon Metabolism and Neuro-Psychiatric Phenomena in Pellagrins with Beriberi.**—*Science.* 1939. Aug. 11. Vol. 90. No. 2328. p. 141.

KATZENELLENBOGEN (I.). **Nicotinic Acid in Endemic Glossitis.**—*Lancet.* 1939. June 3. pp. 1260–1262. [13 refs.]

In 1928 the author published an account of what he referred to as epidemic glossitis in which he incriminated the pneumococcus as playing an important rôle [this *Bulletin*, 1928, Vol. 25, p. 996]. In subsequent years the number of cases fell but in November and December of 1938 there was a considerable increase. The glossitis is associated with soreness at the angles of the mouth and salivation and sore throat. The reviewer in collecting together a number of conditions having symptoms analogous to pellagra drew attention to Katzenellenbogen's observations, but that author has never observed the appearance of other pellagrous manifestations in his cases. He however determined to try out the effect of nicotinic acid in his more recent cases and gives case notes of six patients thus treated.

Altogether 24 patients were submitted to nicotinic acid therapy—50 mgm. being given 3 or 4 times a day. In 21 the symptoms disappeared, in 3 no improvement resulted. In one refractory case the same dose was given 8 times a day with no improvement.

The condition is therefore now considered to be due to a deficiency in nicotinic acid but no explanation is offered for the failures.

[It would be interesting to see what effect riboflavin either alone or in combination with nicotinic acid would have on these cases.]

*H. S. S.*

VILTER (Richard W.) & SPIES (Tom D.). **Antipellagric Properties of Quinolinic Acid.**—*Lancet.* 1939. Aug. 19. p. 423.

Quinolinic acid, the 2 : 3-dicarboxylic acid of pyridine has been reported as non-effective in curing canine black tongue by WOOLLEY, STRONG, MADDEN and ELVEHJEM (1938). It has however been shown by DORFMAN, KOSER and SAUNDERS (1938) and the authors to be an effective growth factor for the dysentery bacillus in synthetic amino-acid medium.

It was decided to study the response of seven selected cases of pellagra in relapse to this substance. One thousand mgm. in divided

doses over a period of five hours was administered orally to 6 cases. The response was dramatic; the fiery glossitis faded within six hours of the first dose, the mucous membrane of the mouth regained its normal appearance at the end of twenty-four hours. The patients reported increased strength and sense of well-being. One case exhibiting mental confusion and nervous instability was mentally normal in twenty-four hours.

In all of seven cases the concentration of co-enzymes I and II in the blood rose to normal in twenty-four hours. This study demonstrates a biological difference between human pellagra and canine black tongue.

Previously another biological difference had been shown by SPIES and co-workers (1938) in that pigments soluble in ether and having a reddish purple colour in 25 per cent. HCl appear in the urine of pellagrins in relapse but not in the urine of dogs with black tongue.

It would appear therefore that all the organisms which require pyridine nucleotides for normal cell respiration do not necessarily use the same pyridine derivatives for the biological synthesis of those nucleotides.

[It will be noted that response of the glossitis and stomatitis, and in one case mental confusion, only is mentioned, other symptoms if any receive no comment.] *H. S. S.*

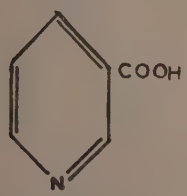
BILLS (Charles E.), MCDONALD (Francis G.) & SPIES (Tom D.). **Anti-pellagric Action of Pyrazine-2, 3-Dicarboxylic Acid and Pyrazine Monocarboxylic Acid.**—*Southern Med. Jl.* 1939. Aug. Vol. 32. No. 8. pp. 793–795. With 1 fig.

In a previous paper the antipellagra activity of certain of the pyridine carboxylic acids was described [see this *Bulletin*, 1939, Vol. 36, p. 557]. The present article deals with the effects of carboxylic acid derivatives of pyrazine, a substance containing two nitrogen atoms in the ring instead of one as in pyridine, and one which is not known to occur in any physiological substance or in any known vitamin, though reduced pyrazine derivatives have been found.

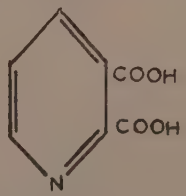
The preparation used was pyrazine-2, 3-dicarboxylic acid the homologue of quinolinic acid, dealt with above, in doses of 100 mgm. five times a day, a dosage which was found non-toxic in volunteers.

Six cases of mild pellagra in relapse were so treated. It is merely stated that a sense of well being was experienced and the glossitis relieved in 2–24 hours.

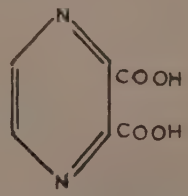
Pyrazine mono-carboxylic acid was also found to yield the same favourable response. Both the substances produce an increase in the co-enzyme I (cozymase) and co-enzyme II (coferment) content of blood and urine [see this *Bulletin*, 1939, Vol. 36, p. 548].



Nicotinic Acid



Quinolinic Acid



Pyrazine-2, 3-dicarboxylic acid

*H. S. S.*

IONESCU (N. Gruia), CLAUDIAN (I.) & CONSTANTINESCU (P.). A propos du traitement de la pellagre par l'histidine. [**The Treatment of Pellagra with Histidine.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Bucarest.* 1939. Nov.–Dec. Vol. 21. No. 9–10. pp. 505–513.

An article in which the authors criticize the results claimed by I. BOGDAN in the treatment of pellagra by histidine.

The treatment adopted in the majority of some ninety cases was 10 daily intramuscular injections of 0,200 mgm. (*sic*) histidine.

The present authors have been unable to confirm the brilliant results claimed by Bogdan. They found " no favourable influence on the clinical symptoms of pellagra " in 15 cases treated. They point out that Bogdan's cases were all treated in the months of April, May and June and that the duration of symptoms was not mentioned by him. It seemed possible that nothing more than a natural ending to the " attack " was observed. *H. S. S.*

BANDIER (Erik). **On the Treatment of Exogenous Pellagra with Stomach Preparations, and Considerations on the Possible Identity of the Vitamin $B_2$ Complex with the " Cyanide Insensitive Enzyme Complex."**—*Acta Med. Scandinavica.* 1939. Vol. 101. No. 4–6. pp. 496–510. [19 refs.]

Two years ago, consequent upon some animal experimental work, PETRI and his associates put to the test the treatment, in Copenhagen, of what the author calls " endogenous " pellagra (*i.e.* pellagra associated with some pre-existing gastro-intestinal dysfunction) with human gastric juice and ventriculin-hydrochloric acid. The results were excellent, pellagrous symptoms disappeared within a month [see this *Bulletin*, 1938, Vol. 35, p. 316].

The present paper deals with the results obtained in 16 cases of endemic pellagra (" exogenous " pellagra of the author) treated in Moldavia, where 4 to 6 per cent. of the population show signs of the disease.

To seven patients ventriculin gm. 10 plus hydrochloric acid (7 per cent.) m. 25 were given thrice daily at mealtimes. Of another group of nine patients : to 3 was given the treatment as above ; to 3 Fundin was given with hydrochloric acid, to 3 Pylorin with acid—all prepared from pig's stomach. The first group of patients all showed typical dermatitis, stomatitis, glossitis, achlorhydria and gastro-intestinal disturbance but no nervous signs and no mental symptoms. All responded to treatment.

The second group were only under observation for a short time but again all showed good response. Though the cases are few in number and there were no controls it is claimed that the reaction to this treatment was prompt and definite.

In the second part of the paper the author refers to some of the results obtained in the United States with nicotinic acid and riboflavine and to facts elucidated by others in regard to the part played by certain fractions of liver extract adding that " it seems a near call to assume that the substance termed the vitamin $B_2$ complex is identical with the so-called 'cyanide insensitive system'," *i.e.* an enzyme complex which comprises : (1) The yellow respiration ferment (Warburg and Christian) . . . . , (2) The co-ferment (Warburg and Christian)

or co-zymase (Euler, Albers and Sclenk) . . . . , (3) The so-called "Zwischenferment."

[This "long shot" is unquestionably near the truth as will shortly be demonstrated.] *H. S. S.*

SPIES (Tom D.). **A Note on the Ocular Symptoms occurring from Malnutrition in Human Beings.**—*Amer. Jl. Med. Sci.* 1939. July. Vol. 198. No. 1. pp. 40–41.

The value of synthetic nicotinic acid, thiamin hydrochloride and riboflavin may now be regarded as established in pellagra and other conditions of vitamin deficiency. Professor Spies has now treated in the same way 50 patients with ocular symptoms—burning, itching, dryness, photophobia in sunlight, some degree of granulation, difficulty in reading from a "film" over the eyes. Great improvement, disappearance of photophobia and burning, amelioration of general health, has followed the daily administration of vitamin A, as carotene in oil, in amounts ranging between 10,000 and 50,000 units.

*H. H. S.*

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## TROPICAL OPHTHALMOLOGY.

### A REVIEW OF RECENT ARTICLES. XXXV.*

HALLAY[1] recommends a novel but simple treatment for surface ocular inflammations due to infection, viz., the application of soap lather. This is said to act as a buffer and restore the acid-base balance in the infected area. Some smarting is naturally experienced and several applications may be required unless the infection is a very recent one.

*Trachoma.*—POLEFF[2] has given a further account with microphotographs of his researches into the tissue-culture of trachoma [see this *Bulletin*, 1939, Vol. 36, p. 956]. From his observations he concludes that the parasitic atoms probably belong to the class of ultraviruses and that the Rickettsia-like corpuscles described by BUSACA and CUÉNOD are identical with Halberstaedter-Prowazek inclusions. The incidence of trachoma in countries commonly considered to be non-trachomatous was the subject of a discussion at the International Organization against Trachoma.[3] LAVERY stated that in Ireland the disease is rare amongst the well-to-do. Some of the orphanages are rather heavily infected. One large institution was badly infected eight years ago, but, owing to improved hygiene, is to-day entirely free.

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* For the 34th of this series see Vol. 36, pp. 955–957.

[1] HALLAY (L. T.). Oligoseptic Treatment of Ocular Infection.—*Amer. Jl. Ophthalm.* 1939. Sept. Vol. 22. No. 9. pp. 1012–1014.

[2] POLEFF (L.). Culture *in vitro* of the Corpuscles of Trachoma.—*Brit. Jl. Ophthalm.* 1939. Nov. Vol. 23. No. 11. pp. 730–740. With 5 figs.

[3] REVUE INTERNATIONALE DU TRACHOME. 1939. July. Vol. 16. No. 3. pp. 137–173.—International Organization against Trachoma. Annual Meeting, April 21st, 1939. Communications from Dr. F. J. LAVERY (Ireland); Dr. Harry GRADLE (United States); Arnold SORSBY (England); Dr. W. ROHRSCHNEIDER (Germany); Paul J. PETIT (France) and others.

A similar institution, however, which lacks adequate facilities for open-air recreation, shows no improvement despite every attention to hygiene. Foci of the disease exist amongst the general population in some of the rural districts; these seem to affect families and the infection does not spread to the schools. It is suggested that this is due to the fact that the schools are unprovided with washing facilities so that there is no community washing. In the year 1937 thirty-five cases were detected amongst 18,868 school-children examined, and in the following year sixty amongst 21,924. Acute trachoma does not occur, but phlyctenular ophthalmia is a common complication. GRADLE estimated that at least 35,000 non-Indians and 25,000 Indians in the U.S.A. were trachomatous. The Indian tribes in the south-west are those chiefly affected. As regards London SORSBY has noticed a steady amelioration owing to the excellent municipal services provided. He considers that unilateral infections are not rare, and has failed to find nasal sepsis a factor in such cases. ROHRSCHNEIDER stated that in Germany the disease was endemic in a few districts only; these mostly lie on the eastern frontier and the poorer classes are the chief sufferers. Trachomatous areas frequently are comparatively louse-free. RADLO and ROSTKOWSKI[4] in view of the supposed virus causation of trachoma studied the Weil-Felix and the Weigl reactions in 320 trachomatous subjects and found the former negative in 92 per cent. and the latter negative in 86 per cent. This compares with 94 per cent. and 87 per cent. respectively in 205 non-trachomatous controls.

BURNET, CUÉNOD and NATAF[5] write with much enthusiasm of their success in the treatment of trachoma by a new preparation of sulphamide (azoique sulfamide No. 33). Struck by its efficacy in experimental lymphogranuloma, the authors thought it might prove equally successful in trachoma. They employed doses of 0·5 gm. four or five times daily by the mouth, and from 1 to 1·5 cc. of a one per cent. solution for subconjunctival injection. Oral therapy alone, however, has been found quite efficacious and injections are unnecessary. Corneal lesions respond in a few days, but conjunctival improvement is less rapid and may not set in until sixty or seventy grammes of the drug have been taken. Once the improvement has started the treatment should be continued intermittently.

*Cornea.*—RHODES[6] has investigated the bacteriology of hypopyon ulcer seen in 120 patients at the Eye Department of the Royal Infirmary, Edinburgh. No fewer than 67 per cent. of these were miners. The investigation brought out two noticeable features: firstly, in 21·6 per cent. the cultures proved negative, and secondly, in only 11·6 per cent. were pneumococci found. The organisms most commonly isolated were diphtheroid bacilli and *Staphylococcus albus*; these, of course, are not necessarily pathogenic. The observer concludes that the result of his investigation tends to minimize the purely infective element in hypopyon ulcer and that three variable factors in its causation must be considered: (1) the bacterial flora of the

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[4] RADLO (Pierre) & ROSTKOWSKI (Louis). Recherches sérologiques du trachome.—*Rev. Internat. du Trachome.* 1939. July. Vol. 16. No. 3. pp. 128–135.

[5] BURNET (Et.), CUÉNOD (A.) & NATAF (R.). Chimiothérapie du trachome par l'azoïque sulfamidé No. 33.—*Bull. Acad. Méd.* 1939. Oct. 17 & 24. 103rd Year. 3rd Ser. Vol. 122. No. 30. pp. 330–342.

[6] RHODES (A. J.). Studies on the Bacteriology of Hypopyon Ulcer.—*Brit. Jl. Ophthalm.* 1939. Sept. Vol. 23. No. 9. pp. 627–631.

conjunctival sac of the traumatized eye; (2) the nature of the traumatizing particle; (3) the resistance of the corneal tissue to infection. [The reviewer's experience in Madras led him to believe that there the two most important factors were the presence of pneumococci and depreciated general health. Slight trauma was sufficient to cause an ulcer if these factors existed. In a high percentage of cases infection was derived from the lachrymal sac.] KIRWAN[7] has reported a case of corneal grafting in which normal vision was obtained in an eye blind from interstitial keratitis. The diameter of the graft was 4·5 mm., and that of the trephine hole in the recipient's cornea was 4·75 mm. The graft was kept in place by two fine silk cross sutures, one arranged in the form of a cross and the other in the form of an X. The sutures were passed through the opaque cornea adjacent to the site of the graft but did not perforate the cornea. They were removed on the fifth day. Seven months after the operation vision was 6/6. Eyes of donors blind from glaucoma furnish good grafts and it is unnecessary to choose a donor of the correct blood group.

*Filariasis.*—McMULLEN[8] has observed *Microfilariae bancrofti* in the aqueous humour of a Hindu student aged 25 living in London. The parasites were first detected in the left eye after a somewhat persistent uveitis had subsided. Six months later the right eye was attacked and a number of microfilariae appeared in the anterior chamber when the eye had quieted. The parasites were never seen during the acute phase of an attack. Fair numbers of *Microfilariae bancrofti* were present in the patient's peripheral circulation at night, but other signs of filariasis were absent. The question arose whether the organisms were the actual cause of the uveitis or whether the inflammation was responsible for their appearance in the eyes. McMullen very plausibly suggested that microfilariae may often be present at night in the aqueous of infected persons with otherwise normal eyes. They disappear, however, in the daytime or when the eye is brightly illuminated for examination. LEVY[9] has reported a case of *onchocercal keratitis* and *cyclitis* in a European resident for ten years in Kenya. Trouble commenced with a persistent chronic conjunctivitis and two years later an established keratitis and cyclitis was found. The corneal infiltration lay at different levels in the substantia. Small foci occurred in the periphery and these coalesced and formed larger plaques. A large area in the centre of the cornea was affected. Heavy keratic precipitates were present, but the iris appeared to be quite healthy. Persistent and troublesome photophobia was a marked feature. No microfilariae were seen nor were there any of the usual subcutaneous nodules; indeed a high eosinophilia seems to have been the only indication of filarial infection.

Steady progress is recorded in the Twenty-fifth Annual Report of the Ophthalmic Hospital Section of the Egyptian Government

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[7] KIRWAN (E. O'G.). Transplantation of the Cornea.—*Arch. Ophthalm.* 1939. July. Vol. 22. pp. 21–24. With 2 figs.

[8] McMULLEN (W. H.). Ocular Filariasis.—*Trans. Ophthalm. Soc. United Kingdom.* 1939. Vol. 59. Pt. 2. pp. 587–601. [15 refs.]

[9] LEVY (A. H.). A Case of Bilateral Keratitis and Cyclitis due to Filaria (*Onchocerca volvulus*) Infection in a European from Kenya.—*Proc. Roy. Soc. Med.* 1939. Oct. Vol. 32. No. 12. pp. 1620–1621 (Sect. Ophthalmology pp. 80–81.)

for the year 1937[10]. The rate of increase in new patients was 7 per cent. and these reached a total of 1,213,781; 5·8 per cent. of those seeking advice were blind in one or both eyes. Acute ophthalmia was the cause in 80 per cent. and the gonococcus was the chief cause of acute ophthalmia. Ninety-nine per cent. of school-children were found to suffer from trachoma in some form. *H. Kirkpatrick.*

[10] EGYPT: MINISTRY OF PUBLIC HEALTH. Ophthalmic Hospitals Section. Twenty-Fifth Annual Report of the Ophthalmic Hospital Section for 1937.—47 pp. With 1 folding map & 1 folding chart. 1939. Cairo: Al-Ettemad Press. [P.T. 10.]

## MALARIA.

### *PRÉCIS* OF ABSTRACTS IN THIS SECTION.

JAKUSHEVA (p. 451) states that in N. Russia only 30 per cent. of the cases occurring in the first half of the year (which is the peak period) are relapses, the remainder being primary infections from the preceding autumn, with prolonged incubation. In S. Russia prolonged incubation is rare and the majority of cases occur in summer-autumn. PANSINI (p. 452) discusses the malaria in labourers repatriated from Italian East Africa. *P. vivax* was the commonest infection. CORRADETTI (p. 452) reports on malaria in Eritrea.

MOSNA (p. 453) discusses the similarities and differences between Ethiopian and Roman strains of *P. falciparum.*

LEESON (p. 453) shows that at 25°C. and after one blood meal the life of female *A. maculipennis* race *atroparvus* is increasingly prolonged with increasing humidity. LEWIS (p. 454) discusses the habits of certain varieties of *A. maculipennis* in Albania. BARROWMAN (p. 454) discusses the effects of the replanting of rubber on the habits and breeding of Anopheles. VENHUIS (p. 455) notes that in Java *A. barbirostris* is a wild species not yet found infected, but in Celebes it is domestic in habit and was infected to the extent of 13·3 per cent. There are also certain minor differences.

ROCCHI (p. 455) quotes experiments which he considers to prove that malaria pigment possesses antigenic power.

HUTTON and SHUTE (p. 456) show that persons who have lived in areas in which malaria is endemic should not be used as blood donors if others are available. Latent infection cannot be diagnosed by any known method and *P. malariae* may persist for many years. GREIG and NEILL (p. 456) show that the incubation period of *P. vivax* infections after inoculation varies from 2 to 24 days, being shortest after intravenous injection, but that, as with *P. malariae*, the number of parasites in the blood of the donor is not correlated with the incubation period.

BOSE *et al.* (p. 456) reveal considerable variations in the quinine content of a number of mixtures, tablets and powders on the market, compared with their stated strengths, and point out that some form of State control is advisable. PIORKOWSKI (p. 457) records a case of agranulocytosis following administration of atebrin to a patient who had been in the habit of taking phenacetin and veramon. MOLLARET

and SCHNEIDER (p. 457) discuss the "dysgonic" action of rhodopraequine which in three daily 3 cgm. doses after about nine paroxysms of induced malaria arrests the attacks for a time. Further paroxysms occur later, after which the parasites lose the power to segment and the infection remains latent for some months. DE SOUSA (p. 458) reports on Quinarsol in treatment.

BARROWMAN (p. 458) shows that the effective life of two drainage pipe lines laid one above the other in the vicinity of trees is more than six times that of the usual single line. GIACOBBE (p. 458) writes of the success of the programme of levelling, Paris green and oil application in controlling malaria in Carbonia, Sardinia.

DECOURT *et al.* (p. 458) show that in fowls infected with *P. gallinaceum* there occurs a phase when, after being infective, the blood, though still containing parasites, is non-infective to other fowls. UNGO-MUGDAN (p. 459) shows that the Feulgen nuclear reaction is positive only in mature schizonts of *P. gallinaceum*. CHORTIS (p. 459) considers that in *P. gallinaceum* infections exoerythrocytic schizonts are the result of imperfect phagocytic action of the endothelial cells, which allows the ingested forms to develop instead of destroying them.

RODHAIN and LASSMAN (p. 459) conclude from their investigations that *P. vivax* and *P. gonderi* show a definite preference for immature erythrocytes which is absent in *P. falciparum*, *P. reichenowi*, *P. knowlesi* and *P. cynomolgi*. *C. W.*

DUNCAN (David). **His Majesty's Naval Base, Singapore—its Medical Aspects.**—*Jl. Roy. Nav. Med. Serv.* 1939. Oct. Vol. 25. No. 4. pp. 394–411. With 6 figs., 1 diagram, 5 charts & 1 map.

This is an interesting, though somewhat discursive, account of some of the medical and sanitary problems that have been successfully surmounted during the construction of the Singapore naval base. It contains an account of the vectors of malaria encountered and of the methods of control adopted. The effect of tropical climates on health and efficiency is discussed as are the attractions and drawbacks of service in the tropics. There is a good description of the Cameron Highlands, a Malayan hill-station in process of development, which promises to confer great benefit on Europeans serving in this part of the Far East. The article will be of special interest to naval Medical Officers who are likely to be appointed for duty in Singapore.

*Norman White.*

JAKUSHEVA (A. I.). Types des courbes de la fréquence du paludisme et la relation entre le nombre de cas initials printaniers et la fréquence automnale de l'année précédente. [**Types of Malaria Incidence Curves and the Relation between the Number of Primary Spring Cases and the Autumnal Prevalence during the Previous Year.**]—*Med. Parasit. & Parasitic Dis.* Moscow. 1939. Vol. 8. No. 3. [In Russian pp. 267–286. With 13 figs. [36 refs.] French summary p. 287.]

In the USSR there are two main types of malaria incidence curve: a northern type with a spring–summer maximum, and a southern type in which the maximum incidence is in the summer–autumn, with a slight rise in the spring. An intermediate type of curve also occurs.

In the north more than half the total cases occur in the first half of the year, even up to 75 per cent. in exceptional years. Only some 30 per cent. of the cases occurring in the first half of the year are relapses, the remainder being primary infections with prolonged incubation. Any increase in the number of *P. vivax* infections in the summer and autumn is only made manifest the following spring, in the north and central parts of the USSR.

In the south of the country cases of prolonged incubation are of rare occurrence; the spring rise in the incidence curve is caused by relapses. A thorough treatment of these relapses should have beneficial effect on the summer incidence by diminishing the infection rate of anophelines.

In the north and centre spring relapses also call for thorough treatment but more effective still would it be to find a means of detecting individuals undergoing prolonged incubations and submitting them to appropriate treatment before the spring rise materializes.

*N. W.*

PANSINI (Girolamo). La malaria dei lavoratori reduci dall'Africa Orientale. [**Malaria of Manual Labourers repatriated from East Africa.**]—*Rass. Sociale d. Africa Italiana.* Rome. 1939. June. Vol. 2. No. 6. pp. 710–720.

This is a discussion in somewhat general terms of malaria in Italian East Africa, based on the large experience of the Hospital in Aversa which was created for the benefit of the manual worker invalided home. Of the 7,400 patients admitted into that institution between September 1937 and October 1938, sufferers from malaria numbered 3,500. Emphasis is laid on the very wide diffusion of malaria throughout the territory. Places at high altitudes are not exempt. A table is given of twelve localities situated at heights varying from 1,026 to 2,900 metres at which primary infections of malaria have been acquired.

The cases treated in the hospital were nearly all relapses, the primary infection having been acquired at varying, often very considerable, periods before admission. The preponderance of *P. vivax* infections is noteworthy. Of the 476 patients in whom parasites were found 81 per cent. harboured *P. vivax*, the remainder *P. falciparum*. Double infections were rare, 1 per cent. Many of the patients had been taking prophylactic quinine when first attacked, some of them apparently in regular and in what is generally regarded as sufficient doses. The very large majority of patients are discharged from hospital at Aversa fit for work; the institution is thus doing a work of very great social importance.

The cases were not of outstanding severity. The few cases that displayed unusual symptoms have been described elsewhere in the literature.

*N. W.*

CORRADETTI (Augusto). Ricerche sulla malaria nella *Dancalia meridionale.* [**Malaria in Southern Dancalia.**]—*Riv. di Malariologia.* Sez. I. 1939. Vol. 18. No. 4. pp. 249–255. With 5 figs. (1 map) on 3 plates (1 folding). English summary.

This is an account of observations made along the trade route which runs from Assab, a port on the Red Sea in Eritrea, to Batie.

The route runs south-west, to the north of the River Auasc and crosses several tributaries of that river. Malaria incidence is high during the dry season in the neighbourhood of perennial streams, and throughout the territory during the rains. A total of 3,423 persons was examined: the average parasite rate was 9·8 per cent. The infection rates according to race were, Dancalis 3, Sudanese 6, Arabs 9·6, Italians 13·8, Somalis 14·5 and Abyssinians 18·6 per cent. It is concluded that the race best adapted for labour forces in this territory is the Sudanese; the Dancalis are nomads and but little adapted to labour. *P. falciparum* infections formed 56·8 per cent. of the total, the remainder being *P. vivax* infections. *P. malariae* was not found. The chief malaria vector throughout the area is *A. gambiae*. *A. pharoensis*, *A. pretoriensis* and *A. dancalicus* n. sp were also found. *N. W.*

MOSNA (Ezio). Sulla malaria indotta da *Plasmodium immaculatum* ceppo etiopico e ceppo campagna romana. [**Malaria induced with Ethiopian and Roman Campagna Strains of** *P. falciparum*.]—*Rendiconti Istituto di Sanità Pubblica*. Rome. 1939. Vol. 2. Pt. 2. pp. 489–502. With 10 charts.

Four patients were inoculated intramuscularly with citrated blood infected with an Ethiopian strain of *P. falciparum*, and four other patients similarly infected with a Roman Campagna strain. No appreciable difference was noted between the two strains with regard either to the incubation period, or to their capacity of infecting *A. maculipennis* var. *atroparvus*, or to their morphology. Febrile attacks provoked by the Roman strain were more prolonged and the symptoms were more severe. There is less liability to relapse in infections with the Ethiopian strain. The Ethiopian strain is much more amenable to quinine therapy [see also this *Bulletin*, 1939, Vol. 36, p. 919]. *N. W.*

LEESON (H. S.). **Longevity of** *Anopheles maculipennis* **race** *atroparvus*, **Van Thiel, at Controlled Temperature and Humidity after One Blood Meal.**—*Bull. Entom. Res.* 1939. Nov. Vol. 30. Pt. 3. pp. 295–301. With 2 figs.

The author has exposed adult *Anopheles maculipennis* race *atroparvus* to controlled climatic conditions and records the length of life of females which have received one blood meal and of others which have not been fed.

The material used in these experiments had been bred in London for a number of generations. In spite of the use of a standardized technique, the author discovered that there were large differences between different batches of mosquitoes; these differences may be seasonal, but that is not proved. The female is generally willing to take her first blood meal on the second day, and is thereafter maintained at 25°C. and a controlled humidity until death. It is found that the insects live longer the higher the humidity (and that the same is true of *Culex fatigans*); this point may seem obvious but it has not previously been studied with care. At the highest humidity, 90 per cent., the mean life of the female was 8·3 days and the maximum 14.

Facts are also given on the survival of males and females which have not been fed, the proportion of females which took blood, and the proportion of the sexes among the mosquitoes which were bred.

*P. A. Buxton.*

LEWIS (D. J.). **The Seasonal and Geographical Distribution of *Anopheles maculipennis* in Albania.**—*Riv. di Malariologia.* Sez. I. 1939. Vol. 18. No. 4. pp. 237–248. With 5 text figs. & 4 figs. on 2 plates.

In Albania three varieties of *A. maculipennis* have been distinguished, *A. m. typicus*, *A. m. subalpinus*, *A. m. messeae* and *A. sacharovi*. Marked seasonal changes in the relative frequency of the different forms occur. In summer the eggs of these four varieties conform to their usual appearance, but in spring and autumn many eggs of the first three named varieties cannot be identified with certainty. Eggs of *typicus* are paler in summer than in spring. In the cold weather of early spring and of late autumn the eggs of each variety tend to be darker and the three forms of barred eggs resemble one another closely.

In autumn *A. maculipennis* and *A. sacharovi* leave wattle stables for stone buildings; *typicus* often enters hollow trees. *A. sacharovi* breeds chiefly in brackish water and is rarely found far from the coast. It hibernates less completely than does *A. maculipennis* and it enters stone buildings a month later. It exhibits a certain degree of gonotrophic dissociation. If malaria transmission takes place during winter and early spring *A. sacharovi* might be an efficient vector. *A. m. typicus* lays eggs in many types of water; *subalpinus* and *messeae* show a marked preference for marshes. A relatively high water temperature, or some other factor dependent on scarcity of shade, appears to favour a high rate of emergence in *subalpinus*. The temperature of water appears to be of little importance as a factor determining the selection of a site for egg-laying, of any variety.

*N. W.*

VAN THIEL (P. H.), in collaboration with J. REUTER, J. SAUTET & L. BEVERE. **On Zoophilism and Anthropophilism of Anopheles Biotypes and Species.**—*Acta Leidensia (Scholae Med. Tropicae).* 1939. Vol. 14. pp. 240–276. With 6 figs. [27 refs.]

BARROWMAN (Barclay). **Replanting and Malaria.**—*Jl. Malaya Branch Brit. Med. Assoc.* 1939. Sept. Vol. 3. No. 2. pp. 170–174.

This circular was written for the benefit of rubber planters in Malaya, to whom it should be of very great service. Increased malaria resulting from replanting is caused not only by procedures which encourage increased breeding of the mosquito carrier, but also by procedures which disturb its usual habits. As an example of the latter, clearing may well result in the removal of attractive resting-places for *A. maculatus* from the neighbourhood of dwellings; the dwelling itself may then be used as a resting-place. The author states that extended flights of anophelines take place often, if not always, into subsoil-drained or other areas in which there is no actively repellent factor in the control, *e.g.*, oiling. The manner in which replanting creates additional collections of surface water is described as are the ways and means of dealing with them.

*N. W.*

VENHUIS (W. G.). Voorloopige entomologische mededeelingen omtrent *An. barbirostris* van Celebes. [**Preliminary Entomological Communication on** *A. barbirostris* **in the Celebes.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1939. Oct. 3. Vol. 79. No. 40. pp. 2515–2519. English summary.

"The *An. barbirostris* from several places in Celebes is morphologically very near to *An. barb. typ.* from Java.

"However some differences were observed, the most outstanding of them being the fact, that in the Celebes form the white tarsal band between the 3rd and 4th tarsal segment is very narrow and only formed by white scales on the apical part of the 3rd tarsal segment, whereas in *An. barb. typ.* from Java the band is usually a little broader, while the basal part of the 4th tarsal segment is white as well.

"In the larva from Celebes the number of branches of several hairs is a little smaller than in Java, but a good difference for practical use has not yet been found.

"It is very interesting that the anal gills in the larva from Malekoe (Celebes) are very much longer than in Java. The length of these gills of the larvae from other places lies between these two extremes. There seems to be no correlation with the amount of chlorine in the breeding places.

"In view of the great difference in feeding habits between the forms from Java and Celebes, so that the *An. barbirostris typ.* from Java lives almost as a wild species and was never found infected, whereas the one from Celebes is easily captured in great numbers in houses and proved to be infected for 13·3 per cent. out of over 500 dissections, I am inclined to consider the Celebes form of *An. barbirostris typicus* as different from the Java form. For the name of the Celebes variety 'vanus' ought to be chosen, because of the old name *An. vanus*, given in 1860 by Walker to a mosquito captured at Makassar (Celebes) and which usually is considered to be a specimen of *An. barbirostris*.

"Some slight differences were observed between the *An. barbirostris* from different places in Celebes.

"When the entomological work on this interesting material is completed, the subject will be treated more in detail."

ROCCHI (Filippo). Valore antigene del pigmento malarico. [**Antigenic Power of Malaria Pigment.**]—*Riv. di Malariologia.* Sez. I. 1939. Vol. 18. No. 4. pp. 225–236. English summary.

The malaria pigment used by the author in his experiments was obtained from two spleens, one from a man who died from malignant tertian malaria, the other a large spleen removed by splenectomy from a patient with chronic malaria. The method used for the isolation of the pigment is described in detail. For skin reactions the pigment was dissolved in a solvent composed of a saturated solution of lithium carbonate 1·3 parts; physiological salt solution 10 parts. Injected intradermally into the skin of a rabbit a large maculo-papule results some three hours later and persists for about six hours. Eight rabbits which gave this positive reaction received on alternate days intravenous injections each of 0·5 cc. of the pigment solution. Every fourth day the intradermal test was repeated. In each case, after the 5th or 6th injection, the intradermal reaction became negative and remained so for many days. The serum of such rabbits gave a positive flocculation test, the solution of malaria pigment being used as an antigen. Intradermal tests on man give similar results. Malaria pigment used as an antigen in Henry's reaction was used with success.

Malaria pigment is soluble in plasma. On the basis of these observations the author considers the antigenic power of malaria pigment as established. *N. W.*

HUTTON (E. L.) & SHUTE (P. G.). **The Risk of transmitting Malaria by Blood Transfusion.**—*Jl. Trop. Med. & Hyg.* 1939. Oct. 16. Vol. 42. No. 20. pp. 309–312.

The authors' remarks on the risk of transmitting malaria by blood transfusion are based for the most part on their observations on malaria induced by infected mosquitoes. *P. vivax* may persist in the blood for 18 months after the primary infection: *P. falciparum* for at least 12 months, and *P. malariae* for many years. Latent cases of malaria cannot be diagnosed with certainty by any known method. Persons in apparent good health may harbour parasites in sufficient quantity to transmit malaria if they serve as donors for blood transfusion. Persons who have lived in areas in which malaria is endemic should not be used as donors if others are available. If such persons must be used as donors the risk of their blood transmitting malaria may be much lessened if they take quinine, ten grains a week, regularly. Keeping the donor's blood for days, or even weeks, at low temperatures, will not destroy the Plasmodia it may contain. *N. W.*

GREIG (E. D. W.) & NEILL (Alexander). **Observations on the Incubation Period in Cases of Induced Malaria.**—*Jl. Trop. Med. & Hyg.* 1939. Nov. 1. Vol. 42. No. 21. pp. 325–328. With 5 charts.

The observations concern cases of malaria in which infection was induced by the inoculation of parasites by the intravenous, intramuscular or subcutaneous routes. The incubation period is the interval between the inoculation and the first appearance of parasites in the peripheral blood. In 144 *P. vivax* infections the incubation period varied from 2 to 24 days, average 6·8 days. The incubation period was shortened considerably when the parasites were introduced intravenously. This is a point of practical importance in malaria therapy: intravenous injection did not affect any of the 84 patients injuriously. The number of parasites in the blood of the donor does not appear to be correlated with the length of the incubation period. Nine cases were inoculated with *P. malariae*. The average incubation period was 14·1 days. Here again the number of parasites injected was not correlated with the duration of the incubation period. Fifteen cases were inoculated with *P. knowlesi*. Incubation periods varied from 3 to 20 days, average 7·6 days. In three cases infection failed to materialize. *N. W.*

BOSE (Indu Bhusan), MUKERJI (B.) & CHOPRA (R. N.). **Quality of Quinine Preparations in Indian Hospitals and Dispensaries.**—*Indian Med. Gaz.* 1939. Oct. Vol. 74. No. 10. pp. 609–613.

One hundred samples of "quinine mixtures" were analysed: 64 of these showed a deficiency of quinine; 16 contained more quinine than they should have done. Of forty samples of quinine tablets, both Indian and foreign, half had a deficient quinine content. Of 28 samples of quinine sulphate, febrifuge powders, etc., 13 were below standard: quinine sulphate powders contained adulterants. The

investigation reveals a very unsatisfactory state of affairs which appears to justify the authors' demand for some form of State control. The matter is one of great public health importance. *N. W.*

PIORKOWSKI (F. O.). **Agranulocytosis after Atebrin Treatment.**—*East African Med. Jl.* 1939. Sept. Vol. 16. No. 6. pp. 227–231.

A woman with a long history of many diseases, including malaria, was operated on for a purulent discharge of the antrum. After the operation a sudden rise of temperature was thought to have been possibly due to a relapse of malaria and the patient received an intramuscular injection of atebrin 0·3 gm. on each of two successive days, and the same dose by mouth on each of the next two days. Phenacetin was given to relieve persistent headache: the patient was accustomed to take this drug, in considerable quantities, as well as veramon. The patient's condition grew worse, and on the 7th day after the operation the diagnosis of agranulocytosis was made. The number of white cells was only 2,100 per c.mm., 86 per cent. of which were lymphocytes and 14 per cent. monocytes. There was a complete absence of granulocytes. Under treatment with sodium pentnucleotide the patient eventually recovered. The author considers it probable that a prolonged use of phenacetin and veramon was the primary cause of the agranulocytosis, and that the shock of operation and the following atebrin treatment aggravated the condition. *N. W.*

MOLLARET (P.) & SCHNEIDER (J.). Une nouvelle méthode d'impaludation thérapeutique. L'impaludation en deux temps, sans réinoculation mais avec apyrexie intermédiaire et récurrence ultérieure réglables à volonté. [**A New Method of applying Malaria therapeutically.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1940. Jan. 3. 55th Year. 3rd Ser. No. 27. pp. 1336–1339. [Summary appears also in *Bulletin of Hygiene.*]

The method suggested is the outcome of work carried on regarding the action of synthetic drugs, essentially gametocide, on *P. vivax.* The drug which in the authors' hands has given constant results is a mixture in equal parts of praequine (6-methoxy-8-diethylamine-isopentyl-amino-quinoline) and rhodoquine (the same except that propyl replaces isopentyl); they call the combination rhodopraequine and administer it subcutaneously. They find that injection of 3 cgm. on three consecutive days after the usual series of paroxysms—nine as a rule—arrests these, except for one single mild attack which may follow. There succeeds an apyrexial period during which no parasites—gametocytes or schizonts—can be found in the blood, but they have not been destroyed entirely, for attacks will return spontaneously or may be provoked by injection of 20 cc. of the patient's own blood. Parasites reappear in the blood, at first schizonts, later sexual forms; after 3 or 4 attacks the fever spontaneously comes to an end and, say the authors, the schizonts have lost all ability to segment and the drug has a "dysgonic" action [see this *Bulletin*, 1939, Vol. 36, p. 498]. After the second apyrexia the patient enters the chronic malarial state, the parasites persist in his blood, but he suffers from no malaria attacks, spontaneous or induced, and this condition persists for 6 months at least, during which his blood, if injected into a fresh subject, will give rise to typical malaria attacks. *H. H. S.*

DE SOUSA (Menino). **Recent Advances in Malarial Therapy.**—*Med. Bull.* Bombay. 1939. Oct. 7. Vol. 7. No. 19. pp. 599–601.

The author reports good results in the treatment of 30 cases of malaria, both tertian and subtertian, with a proprietary preparation called "quinarsol." This is stated to be quinophenyl-dimethyl-pyrazolone-sodium dimethylarsenicum. The dose given was three "tablets" a day for four days, and one tablet a day for the succeeding ten days. [There were no control patients treated with the more usual quinine salts, and no comparative estimate of the value of this drug can therefore be made.] *N. W.*

BARROWMAN (Barclay). **An Expedient in Antimalarial Subsoil Drainage.**—*Jl. Malaya Branch Brit. Med. Assoc.* 1939. Sept. Vol. 3. No. 2. pp. 175–176.

When subsoil pipes are laid near trees they are apt to get choked by roots of trees. In such circumstances it is effective to lay two pipe lines one above the other. In the dry weather such water flow as there may be will be confined to the lower line of pipes: this may become blocked eventually and there will be but a single pipe line functioning. Experience has shown, however, that the effective life of the double line is more than six times longer than that of the usual single line of pipes. In suitable open soils fascine drainage is another alternative for draining soil near trees. *N. W.*

GIACOBBE (Marco). La lotta contro la malaria durante la costruzione della città di Carbonia. [**Anti-Malaria Campaign during the Construction of the Town of Carbonia, Sardinia.**]—*Riv. di Malariologia.* Sez. I. 1939. Vol. 18. No. 4. pp. 256–275. With 2 figs. English summary.

This is a detailed account of the measures that have been taken to control malaria during the construction of the new town of Carbonia. The measures were comprehensive and crowned with success. During nine months from January to September there were 882 cases of malaria; only ten of these were believed to be primary cases, the remainder being relapses. The author considers that success was in large measure due to larval control, levelling, Paris green and oil.

*N. W.*

DECOURT (Philippe), SCHNEIDER (Jean) & KERREST-GROSDIDIER. Disparition du pouvoir infestant du sang pendant la phase descendante de l'infestation par *Plasmodium gallinaceum.* [**Disappearance of Infective Power of the Blood during Declining Phase of** *P. gallinaceum* **Infection.**]—*C. R. Soc. Biol.* 1939. Vol. 131. No. 22. pp. 1193–1195.

By taking blood daily from fowls inoculated intraperitoneally with blood containing *Plasmodium gallinaceum* and inoculating it into other fowls, the authors have shown that the malarial infection has four phases. During the first phase of four or five days' duration the blood of an inoculated fowl is non-infective to other fowls and contains no detectable parasites. In the second phase parasites appear in the blood, which is now infective. After the crisis the parasites begin to decrease

in number and the third phase is reached. The point of the paper is to note that during the third phase though parasites are present in the blood it is non-infective. Following this a fourth phase is reached, during which the blood is again infective, though the number of parasites present may be very small indeed. After this there intervene short non-infective periods from time to time. *C. M. Wenyon.*

UNGO-MUGDAN (Armida). La reazione nucleare di Feulgen negli stadi [? endo-] e exo-eritrocitici del *P. gallinaceum* Brumpt (1935). [**Feulgen Nuclear Reaction in the (Erythrocytic) and Exo-erythrocytic Stages of** *P. gallinaceum*.]—*Rendiconti Istituto di Sanità Pubblica.* Rome. 1939. Vol. 2. Pt. 2. pp. 573–574. With 2 coloured figs. on 1 plate.

The author has tested the Feulgen reaction in various stages of development of *Plasmodium gallinaceum.* The only stages in which it was positive were the mature schizonts, both endo- and exo-erythrocytic forms. In a coloured plate is shown the appearance of both these forms when stained according to the Feulgen technique.

*C. M. W.*

CHORTIS (Panaiotis). Sulle alterazioni del sistema reticolo endoteliale nelle infezioni da *Plasmodium gallinaceum.* [**Changes in the Reticulo-endothelial System in** *P. gallinaceum* **Infections.**]—*Rendiconti Istituto di Sanità Pubblica.* Rome. 1939. Vol. 2. Pt. 2. pp. 445–452. With 2 plates (1 coloured).

The author notes that in acute *Plasmodium gallinaceum* infections in fowls there is a marked proliferation of the reticulo-endothelial system. Fowls die of anaemia which is the result of active destruction of red blood corpuscles by the parasites. If an infection becomes chronic in fowls which recover from the acute infection without quinine treatment the same reaction of the reticulo-endothelial system is observed. The anaemia developed during the acute phase persists as a result of a failure of the blood-forming function. The same type of anaemia is observed in cases in which quinine is administered during the acute phase, but in this case there is no marked reaction on the part of the reticulo-endothelial system. It is concluded that the exoerythrocytic schizonts are the result of an imperfect phagocytic action of the endothelial cells, which allows the ingested forms to develop instead of destroying them. These forms are thus to be regarded as accidental and in no way essential stages of development. *C. M. W.*

RODHAIN (J.) & LASSMAN (P.). Au sujet du comportement différent de divers plasmodiums de mammifères vis-à-vis des réticulocytes. [**Differing Behaviour of Various Plasmodia of Mammals with Regard to the Reticulocytes.**]—*Ann. Soc. Belge de Méd. Trop.* 1939. Sept. 30. Vol. 19. No. 3. pp. 423–444. With 4 figs. on 1 plate. [23 refs.]

The authors have examined the blood of human beings suffering from *Plasmodium falciparum* and *P. vivax* infections and of monkeys or chimpanzees harbouring *P. reichenowi, P. knowlesi, P. cynomolgi* and *P. gonderi* from the point of view of the relative numbers of mature and immature erythrocytes infected. In the case of *P. vivax* in man

and *P. gonderi* in the monkey it was found that from 49 to 248 per thousand of reticulocytes were infected, while with the other parasites never more than 2 per thousand were infected. It is concluded that the young forms of *P. vivax* and *P. gonderi* reveal a definite preference for the immature erythrocytes, in spite of the fact that SIMONS in a recent publication has raised objections of a mathematical nature to the conclusions based on observations of the kind which the paper under review describes. *C. M. W.*

### ERRATUM.

In the summary of the discussion on the paper by CHRISTOPHERS entitled "Malaria in War," this *Bulletin*, 1940, Vol. 37, p. 174, it is reported that WHITTINGHAM (p. 175) advised the use of methylated spirit in preparing Leishman's stain. This was an error in the original account of the discussion. *For* methylated spirit *read* methyl alcohol.

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## VENOMS AND ANTIVENENES.

### *PRÉCIS* OF ABSTRACTS IN THIS SECTION.

MAIER (p. 461) shows that a substance having the trade name Zephiran is an efficient agent for the preservation of toxicity when mixed with venom. DE (p. 461) gives a method for purifying the haemolysin fraction of the venom of *N. naja*. BOQUET (p. 461) gives further details of work on the detoxification of venom by solutions of copper sulphate in the presence of hydrogen peroxide, in this case using the venom of *N. tripudians*.

OH (p. 462) has investigated the effect of common Formosan snake venoms on blood coagulation *in vitro* and *in vivo*. CÉSARI and BOQUET (p. 462) point out the differences between the colourless venom of *V. aspis* from the Department of Gers and the yellow venom found in the same species from other districts.

In discussing the mechanism of the hypotension resulting from injection of cobra venom, GAUTRELET (p. 463) concludes that the action is on the capillaries and coincides with the liberation of histamine. BERTRAND and VLADESCO (p. 463) show that in animals a degree of hyperglycaemia follows the injection of lethal doses of cobra venom. They (p. 463) found the same effect in venoms of both Viperidae and Colubridae and consider that the fraction responsible for this effect is probably distinct from the toxic fraction.

RUTHERFORD (p. 464) reports on the relief of pain following the use of cobra venom, which acts specifically on the pain centres of the cerebrum.

PONNAMBALAM (p. 464) describes a fatal case of krait poisoning.

JÖRG (p. 464) describes poisoning by Bothrops and details the treatment he advises; suction methods are emphasized. CHOPRA and CHOWHAN (p. 466) draw attention to shock due to fear in cases of snake bite; details of early and late treatment are given, with emphasis on suction methods and artificial respiration in the former. ALLEN (p. 466) reports experiments on the local treatment of experimental snake bite in animals and concludes that the Jackson method of multiple incisions and suction is that of choice.

GITHENS and WOLFF (p. 467) show that certain antigenic components are common to many venoms, and to obtain a satisfactory polyvalent antivenene against the common N. American pit vipers one venom from each of three groups mentioned is necessary. There appear to be two distinct neurotoxins in pit viper venoms, one acting on the respiratory apparatus and the other on the voluntary muscles of the body. CÉSARI and BOQUET (p. 467) report satisfactory production of antivenene in rabbits immunized with the venom of *V. aspis*, to which formalin had been added (anavenin). *C. W.*

MAIER (Eugene). **Preservation of Biological Fluids (Bacteriophage Vaccines and Venom Solutions) with Alkyl-Dimethyl-Benzyl-Ammonium-Chloride.**—*Jl. Bacteriology.* 1939. July. Vol. 38. No. 1. pp. 33–39. With 2 figs.

Many snake venoms when kept for experimental work are very unstable, being affected seriously by heat and rapidly losing potency even at room temperature. The author has apparently found a solution of the difficulty. A compound, having the trade name of Zephiran and with a chemical composition alkyl-dimethyl-benzyl-ammonium chloride added to venom to make a final strength of 1 in 50,000—the venom being obtained freshly, then frozen and dried rapidly *in vacuo* over sulphuric acid—caused no loss of toxicity of rattlesnake or moccasin venom when it was tested on mice after six months.

The same concentration (1 in 50,000) was found equally serviceable in the cases of bacteriophage and autogenous vaccines. *H. H. S.*

DE (S. S.). **Studies on Haemolysin of Cobra Venom. Part I. Investigations on the Isolation of Haemolysin from Cobra** (*Naja naja*) **Venom.**—*Indian Jl. Med. Res.* 1939. Oct. Vol. 27. No. 2. pp. 531–536. [10 refs.]

The author gives details of two methods of purifying the haemolysin fraction of the venom of *Naja naja*. The first consists of precipitation with methyl alcohol, fractional precipitation with acetone and removal of the inert proteins by adsorption on ferric hydroxide gel. The second consists of precipitation with 20 per cent. sodium chloride solution, redissolving the precipitate in water, precipitation with metaphosphoric acid and extraction with cold pyridine.

By both methods an eleven-fold concentration of the haemolysin was obtained. The details of the procedures cannot satisfactorily be abstracted and should be consulted in the original. *C. W.*

BOQUET (Paul). Sur le role de quantités infinitésimales de cuivre dans l'atténuation du venin de cobra (*Naja tripudians*) par l'eau oxygénée. [**The Rôle of Small Quantities of Copper in the Attenuation of the Venom of** *Naja tripudians*.]—*C. R. Soc. Biol.* 1939. Vol. 131. No. 22. pp. 1207–1209. With 1 fig.

In previous notes the author [this *Bulletin*, 1939, Vol. 36, p. 860] has shown that viperine venom exposed to the action of hydrogen peroxide in the presence of minute quantities of copper in the form of copper sulphate, is rendered non-toxic in a few hours at 37°C. The venom of the cobra *Naja tripudians* was similarly investigated and was found to lose virulence in the same manner, but more slowly.

The rapidity with which virulence is lost, as in the case of viperine venom, is in proportion to the amount of oxygen available and the concentration of copper sulphate used. With a concentration of 5 mgm. copper per litre, a dilution of $H_2O_2$ (100 volumes) 1/1600 detoxicated the venom in 4 days; with 2·5 mgm. copper, $H_2O_2$ 1/1200 detoxicated in 8 days; and with 1·0 mgm. copper, $H_2O_2$ 1/800 detoxicated in 8 days. In the absence of copper, hydrogen peroxide has no detoxicating action within 4 days, but from the 6th day there is some attenuation if the proportion of hydrogen peroxide is as high as 1 per cent. Venom, alone or with the addition of copper only, remains fully active in the same period. *C. W.*

i. OH (Jintetsu). Experimentelle Untersuchungen ueber den Einfluss der wichtigeren formosanischen Schlangengifte auf die Koagulation des Kaninchenblutes *in vitro*. [**Coagulation of Rabbit Blood by the Common Formosan Snake Venoms** *in vitro*.]—*Japanese Jl. Med. Sci.* IV. Pharm. 1939. June. Vol. 12. No. 1. pp. 31–55. [21 refs.]

ii. ——. Experimentelle Untersuchungen ueber den Einfluss der wichtigeren formosanischen Schlangengifte auf die Koagulation des Kaninchenblutes *in vivo*. [**Coagulation of Rabbit Blood by the Common Formosan Snake Venoms** *in vivo*.]—*Ibid.* pp. 57–78. [31 refs.]

i. Venom dried over sulphuric acid and dissolved (1 in 5) in physiological salt solution was used with fresh or oxalated blood or with solutions of the coagulating elements, in these experiments. Of the 5 venoms tested four—Mucrosquamatus, Ancistrodon, Bungarus and especially Naja—increased the coagulation time. The remaining venom, Gramineus, delayed coagulation in high concentration but accelerated it in medium and low strength. Clot retraction was lessened by all five. Delay in the appearance of the threads of fibrin due to destruction of fibrinogen and early disintegration of fibrin is responsible for the slow clotting, and in the Gramineus venom, which accelerates coagulation in low concentrations, the accelerated coagulation results from the rapid formation of fibrin owing to the presence in the venom of a thrombin-like substance.

ii. Experiments in living rabbits showed parallel results. *C. W.*

CÉSARI (E.) & BOQUET (Paul). Etude sur le venin blanc de *Vipera aspis*. [**Studies on the Colourless Venom of** *Vipera aspis*.]—*Ann. Inst. Pasteur.* 1939. Dec. Vol. 63. No. 6. pp. 592–599.

As has been noted before [this *Bulletin*, 1939, Vol. 36, p. 854] the venom of specimens of *V. aspis* captured in the Department of Gers is colourless, in contrast to the yellow venom obtained from the same species in other parts of France. The authors have made a study of this colourless venom and compare its properties with those of the yellow variety. Colourless venom *in vitro* has less coagulating and haemolytic power than yellow. *In vivo* it does not provoke the severe widespread local necrosis characteristic of the yellow venom, but has stronger neurotoxic action. This neurotoxic action is not destroyed by heating to 70°C. Serum prepared against the colourless venom protects against both varieties.

These findings support those of other workers who have shown that the venom of one species may have different properties in different geographical distributions [see this *Bulletin*, 1938, Vol. 35, p. 431; 1939, Vol. 36, pp. 856, 859]. *C. W.*

GAUTRELET (J.). Le mécanisme de l'hypotension consécutive à l'injection de venin de cobra. [**The Mechanism of Hypotension due to Cobra Venom.**]—*Bull. Acad. Méd.* 1939. Nov. 14 & 21. 103rd Year. 3rd Ser. Vol. 122. No. 32. pp. 412–417. [25 refs.]

This paper is a discussion of the work of many investigators on this subject, and the author concludes that the hypotension observed does not depend upon a direct effect on the heart. The action is not central but peripheral, and the vegetative nervous system is not directly concerned, though it modifies the effect. This action of the venom is essentially exercised upon the capillaries and coincides with the liberation of histamine, probably through the intermediary of lysocithin. [See this *Bulletin*, 1939, Vol. 36, pp. 564, 565.] *C. W.*

TRETHEWIE (E. R.). **Comparison of Haemolysis and Liberation of Histamine by Two Australian Snake Venoms.**—*Australian Jl. Experim. Biol. & Med. Sci.* 1939. June. Vol. 17. Pt. 2. pp. 145–155. With 7 figs.

i. BERTRAND (Gabriel) & VLADESCO (Radu). La glycémie chez le cobaye et le lapin sous l'influence du venin de cobra. [**Glycaemia in Guineapigs and Rabbits Injected with Cobra Venom.**]—*C. R. Acad. Sci.* 1939. Oct. 16. Vol. 209. No. 16. pp. 585–587.

ii. —— & ——. Sur la glycémie du cobaye et du lapin sous l'influence du venin de cobra.—*Ann. Inst. Pasteur.* 1940. Apr. Vol. 64. No. 4. pp. 344–348.

i. Although the symptoms produced in guineapigs and rabbits by lethal doses of cobra venom are not the same, they both show a degree of hyperglycaemia. This was measured in blood taken from the heart before and after the injection, and with smaller doses of venom (1·0 to 1·5 mgm. dry venom) varied between 13·7 and 25·2 per cent. increase. With a dose of 12·0 mgm. in a rabbit the increase was 7·5 per cent.

This phenomenon has not previously been reported, and since the quantities are easily measured, may by further study lead to better comprehension of the action of venom.

ii. This is a fuller account of the work reported above, in which increases in hyperglycaemia amounting to as much as 84 per cent. in guineapigs and 35·7 per cent. in rabbits are recorded. It is shown that the increase is progressive until the death of the animal.

*C. W.*

BERTRAND (Gabriel) & VLADESCO (Radu). L'action hyperglycémiante des venins de serpents. [**Hyperglycaemia due to Snake Venoms.**]—*C. R. Acad. Sci.* 1939. Dec. 4. Vol. 209. No. 23. pp. 818–821.

The authors have now tested the venom of 14 species of snakes, both Viperidae and Colubridae, for the power to increase the glucose

content of the blood of guineapigs injected with fatal doses. Hyperglycaemia was provoked by all the venoms examined if relatively high doses were used, but it was found that the proportion of the substance responsible for this action was not equal in all species. It is probably distinct from the toxic fractions of venom and it produces a hyperglycaemia which increases progressively until death and is most marked in animals given a dose sufficient to kill in a few hours at most. Increases up to 188 per cent. are recorded. *C. W.*

RUTHERFORD (Robert N.). **The Use of Cobra Venom in the Relief of Intractable Pain.**—*New England Jl. of Med.* 1939. Sept. 14. Vol. 221. No. 11. pp. 408–413. [12 refs.]

The numbing and paralysing action of cobra venom is due to a specific effect on the pain centres of the cerebrum. Its action, in small doses, is comparatively slow but persists longer than, for instance, that of morphine. As in the case of digitalis, a period is necessary for saturation if small doses are used. There is no evidence of addiction or of increased tolerance to the drug.

The author gave cobra venom intramuscularly to 17 patients who were suffering from severe chronic pain. Many were the victims of incurable cancer. The venom is distributed in 1·0 cc. ampoules each containing 5 mouse units, and the individual doses varied but the usual maintenance dose after the initial period was about 1·0 cc. daily. Complete or almost complete relief of pain was found in 8, and a considerable relief in 7 others, only 2 being comparatively untouched. A noticeable feature was the mental improvement which followed the easing of the pain. [See also this *Bulletin*, 1938, Vol. 35, pp. 520, 521, 891]. *C. W.*

PONNAMBALAM (C.). **Notes on a Fatal Case of Krait-Poisoning.**—*Ceylon Jl. Sci.* (Sect. D. Med. Sci.). 1939. Sept. 4. Vol. 5. Pt. 2. pp. 37–38.

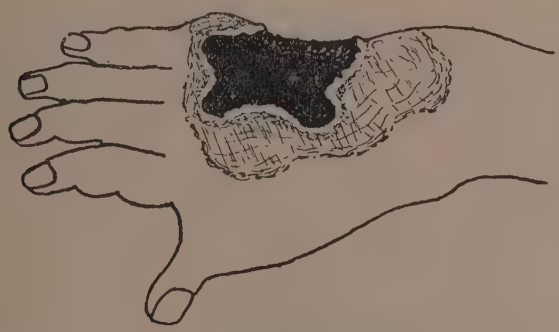
The patient, a woman of 25, was bitten on the hand at 7 p.m. She experienced local burning pain followed by dizziness and general body pain; some local swelling; difficulty in breathing, speaking and swallowing, with loss of taste; drooping of the head and inability to keep the eyes open; copious mucous discharge from mouth and nose and, what is regarded as peculiar to krait poisoning, severe abdominal pain with vomiting. She died 9 hours after the bite. The author points out that as the chief feature of krait poisoning is the action of a neurotoxin on the medulla and on the neuro-muscular junction of the phrenic nerves, death results principally from respiratory paralysis.

The krait (*Bungarus caeruleus*) was identified by the author and its characteristics are given. The patient was treated by a neighbouring ayurvedic physician. *C. W.*

JÖRG (Miguel Eduardo). Ofidismo por serpientes del género *Bothrops*. (Presentación de cuatro casos.) [**Four Cases of Snake-Bite by Bothrops.**]—*9a Reunión Soc. Argentina Patol. Regional, Mendoza, 1, 2, 3 y 4 octubre 1935.* Vol. 3. pp. 1563–1570. With 3 figs.

Of the four described one ended fatally. The patient was a man of 29 years, bitten on the right forearm; he received treatment in

15 minutes, 20 cc. of antivenene intravenously, but died in half an hour with acute oedema of the lungs. Six months previously he had received an injection of antivenene. [From the details given, it is very likely that the acute pulmonary oedema was anaphylactic and not the effect of the venom injected with the bite.] The symptoms are given in a table. One man was bitten on the ulnar aspect of the right hand and the necrosis and sloughing were severe [see figure for state of the lesion 25 days after the bite].



Appearance of lesion 25 days after snake-bite by Bothrops on ulnar aspect of the right hand of a man.

[Reproduced from Vol. 3 of *9a Reunión Soc. Argentina Patol. Regional Mendoza, 1, 2, 3 y 4 octubre 1935.*]

Treatment other than by antivenene is advised as follows: Tourniquet above the site of the wound, free crucial incisions, suction by cupping for 1½ hours, then cease the suction but without removing the tourniquet, and after an hour more suction and repeat this for 20 minutes out of each hour for 15–20 hours. If the oedema has

Correct disposition of crucial incisions around lesion in the surgical treatment of snake-bite.

[Reproduced from Vol. 3 of *9a Reunión Soc. Argentina Patol. Regional, Mendoza, 1, 2, 3 y 4 octubre 1935.*]

extended more crucial incisions are advised. Permanganate of potassium is not advisable as it of itself may cause sloughing.

*H. H. S.*

CHOPRA (R. N.) & CHOWHAN (J. S.). **Snake Bites and their Treatment in India. Part II. The Management of Sequelae and Complications.**—*Indian Med. Gaz.* 1939. July. Vol. 74. No. 7. pp. 422–432. [26 refs.]

This is a full and clear account of the symptoms and treatment of the common snake bites of India. Attention is drawn to the importance of fear shock, which may constitute real danger to life, and a differential table between this and true venom collapse is given, in which it is emphasized that in fear shock the onset is sudden and there is no paralysis, whereas in venom collapse the onset is more gradual and paralysis spreads gradually from the legs upwards.

Immediate treatment is briefly dealt with, and emphasis is laid on methods of suction and on the importance of artificial respiration. For later treatment of respiratory disturbances cardiozol and ephedrine are advocated; for circulatory failure saline infusions and administration of veritol to counteract the histamine-like shock are useful, particularly after viper bites; for haemorrhage calcium and other coagulants and vitamin C may be efficacious.

There follows a section, which cannot be abstracted, on the identification of poisonous snakes and it is pointed out that it is not possible to lay down a brief criterion by which these can be recognized. [See also this *Bulletin*, 1936, Vol. 33, p. 397.] *C. W.*

ALLEN (Frederick M.). **Observations on Local Measures in the Treatment of Snake Bite.**—*Amer. Jl. Trop. Med.* 1939. July. Vol. 19. No. 4. pp. 393–404. [15 refs.]

The author has previously shown that occlusive tourniquets are useless and even harmful in the treatment of snake bite. The present paper is a record of experimental work on 159 rats, rabbits and cats, using the venom of *Crotalus atrox* and *Ancistrodon piscivorus*. It is shown that refrigeration of a limb may be worth a trial for any kind of venom which causes little or no local necrosis, but is contra-indicated for powerful proteolytic venoms. Excision is now largely abandoned since it must be wide to be effective even if performed immediately. It is a promising treatment for smaller bites such as that of the black widow spider. Amputation of the affected limb may be successful if not too long delayed, even after the bite of the king cobra. It is unsafe to delay amputation for as long as 24 hours even when absorption is retarded by a tight tourniquet. The only value of refrigeration or ligation, at least with reference to necrotizing venoms, is that they produce a certain anaesthesia so that operative measures may be undertaken in the absence of an anaesthetic.

The author therefore makes a plea for the wider teaching of mechanical methods of treatment such as the Jackson plan and considers that with proper use mortality from all kinds of venomous bites may be almost abolished. [See this *Bulletin*, 1939, Vol. 36, p. 863.] *C. W.*

GITHENS (Thomas S.) & WOLFF (Nigel O'C.). **The Polyvalency of Crotalidic Antivenins. I. The Influence of the Composition of Polyvalent Antigens. II. Comparison of Polyvalent Crotalidic Antivenin with Monovalent *Crotalus D. Durissus* Antivenin. III. Mice as Test Animals for Study of Antivenins.**—*Jl. Immunology.* 1939. July. Vol. 37. No. 1. pp. 33–39; 41–45; 47–51.

I. Antivenenes prepared against mixtures of various species of Crotalus, Sistrurus and Ancistrodon were found to be efficient in a considerable range, but the efficiency was not determined by the venoms used in the immunizing mixture. For instance, one antivenene was more effective against *Crotalus viridis viridis*, which was not included in the venoms used in its preparation, than against any of those venoms which had been used. Even the venoms of three species of Bothrops were fairly efficiently neutralized though no Bothrops had been used in preparation.

Certain antigenic components are therefore common to many venoms and an antivenene need not be prepared against all the venoms in question so long as enough are present to give a wide antigenic base. "Venoms of North American pit vipers from three antigenic groups: (*a*) most of the rattlesnake venoms; (*b*) venoms capable of causing late paralytic symptoms; (*c*) mocassin venoms. To yield a satisfactory polyvalent antivenin at least one venom from each of these groups must be included in the mixture used for injections of the antivenin-producing animal." The venoms used are listed according to these groups.

II. North American pit viper venoms which induce delayed paralysis are strongly neutralized by a monovalent antivenene prepared against a venom which has this property. This supports the idea that there are two distinct neurotoxic constituents in pit viper venoms. One of these, which is presumably present in all the venoms, acts largely on the respiratory apparatus, the other acts on the voluntary muscles of the entire body. All other North American pit viper venoms are better neutralized by a polyvalent antivenene.

III. Experiments similar to those on which the conclusions of the first two papers were founded were conducted using mice instead of pigeons as the test animals. The results were very similar. With certain viperine venoms other than those used in the work paradoxical results were obtained with the two antivenenes employed and demonstrate further how complex are the antigenic relationships of these venoms. *C. W.*

CÉSARI (E.) & BOQUET (Paul). Production rapide d'un sérum antivenimeux, chez le lapin, au moyen d'un anavenin. [**The Use of Anavenin in the Rapid Production of Antivenene.**]—*C. R. Soc. Biol.* 1939. Vol. 132. No. 25. pp. 363–365.

The antigen used was a 1 per cent. solution of the venom of *Vipera aspis* in a saline to which 4 per 1,000 formol was added (after the method of Ramon). This was kept at 37°C. for 17 days and thereafter at 4°C. After 7 days in the incubator it was no longer toxic for the rabbit in the amount of five times the normal lethal dose. Rabbits were inoculated weekly with this anavenin subcutaneously or intravenously in various doses for varying periods; blood was then taken and mixed with 3 m.l.d. venom for 30 minutes at 37°C. and injected intravenously

into fresh rabbits. It was found that the intravenous method of immunization with anavenin gave higher titres of antivenene than were given by the subcutaneous method although the total doses administered intravenously (61 to 72 mgm.) were smaller than those given subcutaneously (45 to 180 mgm.). In two rabbits 2 cc. serum were enough to neutralize 1 mgm. of the venom.

A number of the rabbits died during, and as a result of, the intravenous immunization with anavenin, but no more than after the higher doses given subcutaneously. Immunization of rabbits with pure venom was almost impossible to obtain owing to death of the animals. *C. W.*

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## REVIEWS AND NOTICES.

WHITE (R. Senior), AUBERTIN (D.) & SMART (J.). **Fauna of British India, Diptera. Vol. VI. Family Calliphoridae.** 1940. London. [18*s*.]

In the present book the authors include not only the Calliphorine flies (*e.g.*, *Calliphora*, *Lucilia*) but also *Chrysomyia*, *Sarcophaga*, as well as many other genera not known to be of medical interest. The book has therefore a distinct value to medical entomologists, because some of the insects included in it have habits like those of the house fly, visiting human food but also feeding on deposits of faeces, and others cause myiasis, either primary or secondary. The introduction includes a good general account of the external anatomy of these flies: with it and the illustrations of diagnostic points anyone with a general knowledge of the anatomy of Diptera could make precise identifications, at least in the majority of cases. The authors' main interest is systematic, but short notes on early stages and biology are given when anything is known. They have included in their area not only India but the rest of the Oriental Region, which includes the Malay Archipelago, Siam, Indo-China and Southern China. As many of the species are very widely distributed the book would also have considerable value to an entomologist working in Tropical Africa.

*P. A. Buxton.*

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